A Report on Various Sleep Drugs Using Bayesian Analysis

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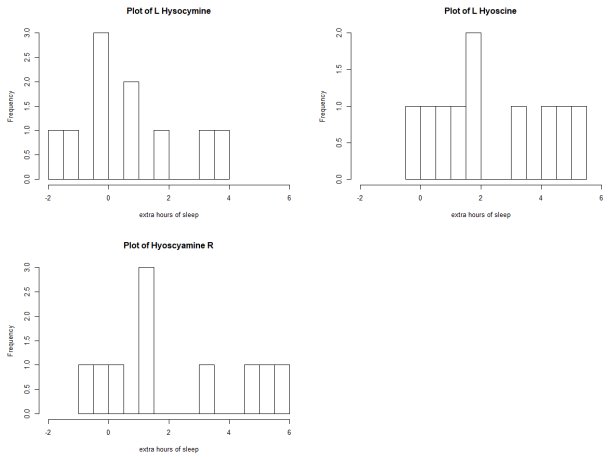
1 Introduction

A study was done testing the efficacy of three different drugs for the use as sleep aids. The study was conducted by medical professionals Arthur Cushny and Roy Peebles. The researches tested the drugs laevorotatory hyoscyamine, laevorotatory hyoscine, and racemic hyoscine on a group of 10 separate patients at the Michigan Asylum for insane at Kalamazoo. First, each patient had their normal average amount of sleep recorded. The journal states, "a tablet was given on each alternate evening, and the duration of sleep and other features noted and compared with those of the interviewing control night on which no hypnotic was given. Hyoscyamine was thus used on three occasions, and then racemic hyoscine, and then laevo-hyoscine. Then a tablet was given each evening for a week or more, the different alkaloids following each other in succession" [1]. Using Bayesian analysis, we will analyze the outcome of this study to determine the how effective each drug is at aiding in sleeping.

2 The Data

The data used contains the average difference in sleep compared to the control group for each patient for 10 different patients. Below is a bar-plot where each bin is separated represents a span of 0.5 hours.



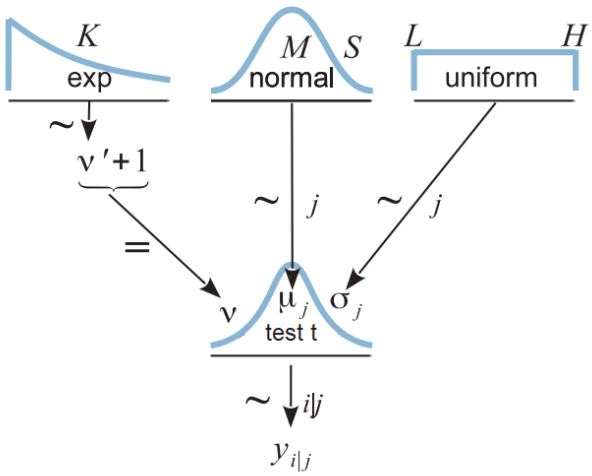
Results of the sleep drug study compared to control group

As we can see, each drug seems to have made some improvement to each patients average sleep. However, we can see that the additional sleep that each patient had due to the drug had a large amount of variance. However, there does seem to be a central tendency towards the center of the distributions. From the plot alone, we can see that L. Hyoscine had the largest overall increase in additional sleep while L. Hyoscyamine had the lowest (in fact it had a decrease in sleep in some cases). We can see that the distributions of the data are slightly skewed.

[1] Cushny Peebles 1905 509

3 The Model

Our model is concerned with finding the distribution of the sleep metric variable. We built a model that finds the posterior distribution of a single test and fit the model to the 3 seperate drug tests. Below is a diagram representing the model that was passed into JAGS:



Bayesian model for building distribution of drug data

In order to account for outliers, this model aims to represent the posterior distribution of the 3 drug tests by using a t-distribution. The parameters for this distribution are sampled from the corresponding distributions in the diagram.

3.1 Prior distribution parameters

The initial distributions that we sample from are based on our prior distribution. The prior distribution parameters are defined from each set of test's data. Our ν parameter was arbitrarily set to 5 to account for the fact that the data is not normally distributed. The mu parameter is set to the average sleep recorded for each test and our sigma set to the corresponding standard deviation. These parameters should get us fairly close to the true posterior distribution. Below is the R code that defines these parameters.

```
# Initial values of MCMC chains based on data:
mu = mean(y)  #mean of data
sigma = sd(y) #sd of data
nu = 5        #arbitrary for t-dist
initsList = list( mu = mu , sigma = sigma , nu)
```

4 The Posterior

4.1 MCMC Diagnostics

We can ensure the accuracy of our posterior distribution due to our MCMC diagnostics. Each of our chains' metrics satisfy the assumptions which provide evidence showing that the chains converged correctly. The chains' all showed random behavior during the run period. All of our chains' auto-correlation and shrink factors converge towards 1 and 0 respectively and our density plots show tightly clustered distributions. If you would like see the diagnostic maps, please refer to the code.

4.2 Establishing ROPE parameters

Considering we are testing the sleep drugs against a control group, we would assume that the drugs should increase the amount of sleep. A reasonable average increase would be an increase in sleep around 2 hours with a range of 0.5 hours in either direction. Accounting for variation, a good sleep medication would probably affect a user at most and hour more or at least an hour less than the average, so we set the ROPE for sigma as 1 with a range of 0.5 hours in either direction. For effect size, the ROPE value was set to 0.2 with a range of 0.1.

4.3 Simulation results

Below are the posterior distributions of the parameters for the 3 different drug tests:

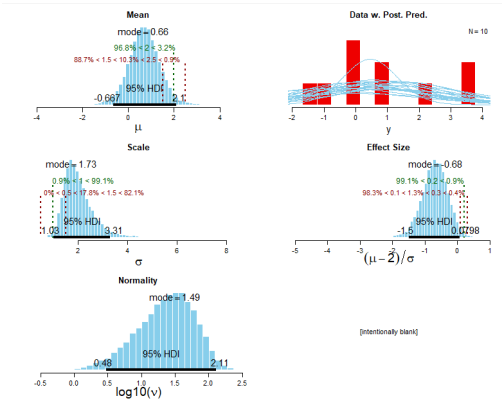


Figure 1: L. Hyoscyamine

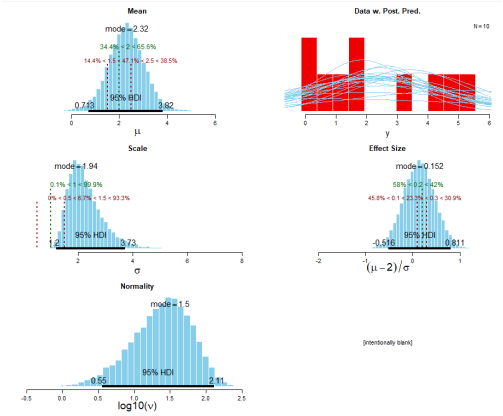


Figure 2: L. Hyoscine

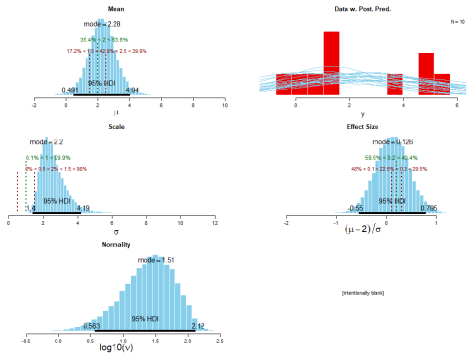


Figure 3: R. Hyoscine

For the drug L. Hyoscyamine, we can see our largest mean value is around 0.66 hours of increased sleep while the range of the HDI is between -0.667 and 2.1. Our ROPE average value falls within this range and can still be considered an effective sleep drug. L. Hysocyamine's variance is centered around 1.73 with an HDI of 1.03 to 3.31. This is also within our ROPE range. The effect size is, however centered around -0.68 and falls outside our ROPE values. Our nu parameter has settled around the value 1.49 suggesting there are outliers.

For L. Hyoscine, our mean is centered around 2.32 hours which is a significant increase over L. Hyoscymine. Our entire ROPE range falls within the 95% HDI which is between 0.713 and 3.92. This shows that this drug is very effective since the HDI contains no negative values. Our variance is larger though being centered around 1.94. The HDI of L. Hyoscine's scale parameter runs from 1.2 to 3.73 which shows that this drug will act a lot differently for different users. The effect size is centers around 0.152 and its HDI runs from

-0.516 to 0.811 which is within the ROPE range. Our nu parameter has settled around the value 1.5 which is almost identical to L. Hyoscyamine.

For R. Hyoscine, our mean is centered around 2.28 with the HDI spanning from 0.491 to 4.04 and our ROPE values sit right in this range. This is evidence suggesting that this may be the best drug as it has the highest average increase in sleep. The scale parameter for R. Hysocine centers around 2.2 with the HDI ranging from 1.4 to 4.19. This drug has the largest amount of variance out of the groups and barely fits within the ROPE range. The effect size is centered at 0.126 with the HDI ranging from -0.55 to 0.785 which is in the ROPE bounds. The normality is also essentially the same as the other two drugs being centered around 1.51.

5 Conclusion

Based on our results, it is evident that the strongest sleep drug that was testing was R. Hyoscine followed by L Hyoscine as a close second. Our HDI and ROPE values agree that these drugs have a significant effect on sleep. It is clear that the data is not very uniform and it may affect the results given that every test yielded a small nu parameter and the large scale parameters. To conclude, either of the two previously afformentioned drugs would be useful in treating sleep. L. Hyoscyamine however, has shown to significantly inferior the the other drugs and would not be recommended to be used for this purpose.

References

[1] Cushny, Arthur R., and A. Roy Peebles. "The Action of Optical Isomers." The Journal of Physiology, vol. 32, no. 5-6, 1905, pp. 501–510., doi:10.1113/jphysiol.1905.sp001097.