1. Regarding the article *Your Brain on Meth: Forest Fire of Carnage*:

(a) (3 pts) The scientific method is:
   
i. Observe some phenomenon
   ii. State a hypothesis explaining the phenomenon
   iii. Collect data
   iv. Analyze the data
   v. Test: Does the data support the hypothesis?
   vi. Conclusion. If the test fails, go back to step ii.

   The scientists in the article followed the scientific method by:
   
i. There are “hazards of drug abuse” for many drugs.
   ii. Paul Thompson at UCLA must have hypothesized that meth use is hazardous to brains. The hypothesis tested in the study reported by *Discover* is that meth addicts have damaged brains.
   iii. High-resolution magnetic resonance images were collected from 22 addicts’ brains.
   iv. *Discover* reported that “Among the 22 addicts whose brains Thompson studied, an average 11.3 percent of limbic cells were destroyed. Both the hippocampus and the cingulate gyrus, two areas of the limbic system associated with memory, showed injury. On average, 7.8 percent of the tissue in the hippocampus, a spoon-size area underneath the frontal lobes, was destroyed ... Surprisingly, methamphetamine addicts brains were about 10 percent larger than normal brains, apparently due to inflammation of the brain’s white matter - the nerve cells that link the different thinking centers of the organ.”
   v. Paul Thompson decided that these results support the hypothesis that meth use adversely affects the brain.
   vi. “That’s why they can’t remember a string of words,” Thompson says. “Its amazing how selective the damage is ... We never found anything like this before.”

(b) (1 pt) The population of interest to the study is meth addicts.

(c) (1 pt) The addicts in the study are likely from a convenience sample (addicts easily contacted by Paul Thompson or one of his collaborators) or a voluntary response sample. UCLA has an award winning medical school. Total speculation on my part: perhaps one of UCLA’s associated clinics treats addicts and asked patients there to participate in the study.

(d) (2 pts) This is an observational study of addicts. A meth treatment was not randomly assigned to some people and then studied.

(e) (1 pt) The two main statistics in the article are that “11.3 percent of limbic cells were destroyed ... [and] on average, 7.8 percent of the tissue in the hippocampus ... was destroyed.”

(f) (3 pts) **Scope of Inference**: This was not a randomized experiment, so it is possible that other behaviors could have caused, or exacerbated, the observed brain damage: other illicit drug use, nutritional deficiencies, lack of regular medical care, and/or physical abuse. Nonetheless, Thompson’s paper in the *The Journal of Neuroscience* explains that the study included inclusion and exclusion criteria in an effort to mitigate these, and other, possible confounding effects. Due to the lack of random sampling, maybe only meth users with brain damage sought to participate in the study. Hence, it would be tenuous to predict the health of other addicts’ brains based on these results. In conclusion, this study shows that these 22 addicts were associated with brain damage.

2. The statistical report for Exercise 25 on page 25 is on the next page.
Introduction

Dieticians are concerned that taking calcium supplements can affect zinc levels. To test this hypothesis, an experiment was performed on 39 rats. Typically, rats for experimental purposes are bred to be genetically be very similar and purchased from specialized companies. Twenty rats received a calcium supplement, the others received no supplement. We will assume that the calcium treatment was randomly assigned. The zinc levels in all rats were then measured - see the side-by-side boxplots in the Appendix.

Statistical Procedures Used

A two-sample two-sided randomization test was used to test for any difference in mean zinc levels between the group of rats that received the calcium treatment (Group A) and the group of rats that did not (Group B); $10^5$ simulations were performed. A histogram of the $10^5$ simulated mean differences is shown in the Appendix. A Welch two-sample two-sided $t$-test was also performed.

Summary of Statistical Findings

The 20 rats in the treatment group that received a calcium supplement (Group A) had slightly lower zinc levels, of $0.078 \text{ mg/ml}$ on the average, compared to the control group (Group B). Results for each group are shown in the following table.

<table>
<thead>
<tr>
<th>Group</th>
<th>A</th>
<th>B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>1.323500</td>
<td>1.4010526</td>
</tr>
<tr>
<td>SD</td>
<td>0.174997</td>
<td>0.2572481</td>
</tr>
<tr>
<td>n</td>
<td>20</td>
<td>19</td>
</tr>
</tbody>
</table>

The difference in means was not statistically significant (randomization test, $p = 0.272$). With 95% confidence, the effect of calcium was between a $0.22 \text{ mg/ml}$ decrease or a $6 \text{ mg/ml}$ increase in mean zinc levels. Similar results were obtained by a Welch two-sample $t$-test ($df = 31$, $p =0.282$, 95% CI for Group A mean - Group B mean: $[-0.22, .06]$).

Scope of Inference

Because these rats were a convenience sample bought from a company, then any conclusions from these data may only hold for the population of rats bred by the company. Because a randomized experiment was performed, the evidence fails to suggest that the calcium supplement caused any change in the mean zinc levels of the rats.

Appendix

In the left pane below, side-by-side boxplots compare the zinc levels (mg/ml) between the group of rats that received the calcium supplement (Group A) and the group of rats that did not receive calcium (Group B) are presented next.

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1. Give an overview of the study’s goal, study design, and sampling plan in the Introduction.
2. Or, I could have stated that the evidence failed to suggest an effect on the mean zinc levels. I would not say there was no evidence of a difference. You could say that there was no evidence of an increase in zinc levels due to the calcium.
3. Explain how study design affects conclusions of cause-and-effect vs. association; and how the sampling plan affects conclusions regarding the population to whom results can be generalized.
The right pane summarizes the results of the randomization test as a histogram of the simulated differences in mean zinc levels (mg/ml) between the group of rats that received the calcium supplement (Group A) and the group of rats that did not receive calcium (Group B). The test statistic value of \( Y_A - Y_B = -0.078 \) is shown by a green vertical line. There is a second green vertical line at +0.078. The area in the histogram in the lower tail (below -0.078) plus the area in the upper tail (above +0.078) is the two-sided p-value = 0.272 for the test of \( H_0 : \mu_A = \mu_B \) vs. \( H_a : \mu_A \neq \mu_B \). The normal approximation, \( N \left( 0, \sqrt{\frac{0.175^2}{20} + \frac{0.257^2}{19}} \right) \), to the histogram representation of the randomization distribution is given by the red bell-shaped curve.

**R-code and R-output**

```r
# Get the data
library(Sleuth3)
rats = ex0125

summary(rats)
## Group   Zinc
## A:20 Min. :1.000
## B:19 1st Qu.:1.165
##      Median :1.330
##      Mean :1.361
##      3rd Qu.:1.525
##      Max. :1.760

# Graph the data
boxplot(rats$Zinc~rats$Group,ylab="zinc (mg/ml)"

# Some simple stats into a table
Mean = tapply(rats$Zinc,rats$Group,mean)
Mean
## A  B
## 1.323500 1.401053

SD = tapply(rats$Zinc,rats$Group,sd)
SD
## A  B
## 0.1749970 0.2572481

n = tapply(rats$Zinc,rats$Group,length)
n
## A  B
```
rbind(Mean,SD,n)
## A   B
##Mean 1.323500 1.401053
##SD   0.174997 0.257248
##n    20.000000 19.000000

# observed difference is 1.323500 - 1.401053 = -0.07755
test.stat = as.numeric(Mean[1] - Mean[2])  # Group A mean - Group B mean
test.stat
## [1] -0.07755263

# How many possible randomizations are there?
choose(39,20)
## [1] 68923264410  # 6.9e10

# Perform 1e5 simulations, a tiny fraction of the total number of randomizations 1e5/6.9e10
num_sim=1e5
diff.mean <- numeric(num_sim)  # storage vector

# generate random assignments and calculate difference in means
for (i in 1:num_sim)
{
  grp<-sample(rats$Group,39,replace=F)
  diff.mean[i]<- mean(rats$Zinc[grp=="A"])- mean(rats$Zinc[grp=="B"])
}

# Graph the approximate randomization distribution
hist(diff.mean,freq=FALSE,ylim=c(0,6),main="Histogram of 100,000 simulated mean differences",
     xlab="mean: Zinc with calcium supplement minus Zinc without")  # a density histogram

# Visualize the test statistic and the p-value
abline(v=test.stat,col=3,lwd=3)  # puts a green vertical line at the test.stat = observed difference
abline(v=-test.stat,col=3,lwd=3)

# Visualize the normal approximation
curve(dnorm(x,0,SE_Unpooled),add=TRUE,col=2, lwd=3)

# Get the two-sided p-value
sum(abs(diff.mean)>=abs(test.stat))/num_sim  # two-sided p-value
## [1] 0.27237

# 95% Confidence interval
quantile(diff.mean + test.stat, p=c(0.025,0.975))
## 2.5%  97.5%
##-0.21463158  0.05939474

# Confirmatory analysis by a t-test
t.test(Zinc ~ Group,data=rats)
##
## Welch Two Sample t-test
##
## data: Zinc by Group
## t = -1.0952, df = 31.532, p-value = 0.2817
## alternative hypothesis: true difference in means is not equal to 0

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95 percent confidence interval:
-0.22187364  0.06676838
sample estimates:
mean in group A  mean in group B
1.323500  1.401053