Analysis of Cisplatin-Induced Neuropathy

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Background

• Chemotherapy drugs are dose limited by their toxicity
• Common treatment period is 3 days
• 30%-40% of all chemotherapy patients experience some kind of neuropathy
Cisplatin

- Causes cross-linking of DNA
- First chemotherapy drug with a platinum core
 Chemotherapy Side Effects

• Chemo-brain (cognitive, memory)
• Auditory problems
• Vestibular problems
• Visual problems
• Neuropathy (pain)
• Rapid heartbeat
• Nausea
Neurons

- Electrically excitable cells
- Respond to stimuli
- Basis for all perception and cognition
Neuropathy
Musk Shrew (*Suncus murinus*)

- Primary small animal model used to study emesis
- Similar vagal pathways to humans
The purpose of experiment is to further study the neuropathophysiology of chemotherapy drugs.
Hypothesis

Null Hypothesis: Cisplatin will not have a significant effect on the nerve morphology of the musk shrew
Procedure

1. The shrews were separated into a control (saline) group and experimental (cisplatin) group individually weighed and injected with a 10mg/kg dose of Cisplatin for 3 days.

2. The subjects were monitored for the 3 days, to ensure that no lethal effect had taken place.

3. Each shrew was anesthetized.

4. In vivo examination was performed on each subject where its vitals were monitored.

5. 3 vagal nerve samples were taken from each shrew.

6. Cross-sections of each nerve samples were made.
Experiment Setup
Nerve Morphology

**Axon density within nerve fibers**

- **Abdominal**
  - Saline: 0.002
  - Cisplatin: 0.004
- **Cervical**
  - Saline: 0.004
  - Cisplatin: 0.006
- **Spinal**
  - Saline: 0.006
  - Cisplatin: 0.006

**Average area of axons**

- **Abdominal**
  - Saline: 15
  - Cisplatin: 30
- **Cervical**
  - Saline: 20
  - Cisplatin: 25
- **Spinal**
  - Saline: 40
  - Cisplatin: 50
Nerve Morphology

Average circularity of axons

- Abdominal
- Cervical
- Spinal

Condition:
- Saline
- Cisplatin

Number of axons per fiber

- Abdominal
- Cervical
- Spinal

Condition:
- Saline
- Cisplatin
T-test

- Parametric statistical test used to determine if two sets of data are significantly different from each other

\[ t = \frac{(\bar{x}_1 - \bar{x}_2) - (\mu_1 - \mu_2)}{\sqrt{\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}}} \]
Data

Axon density within nerve fibers

<table>
<thead>
<tr>
<th>Group</th>
<th>Saline</th>
<th>Cisplatin</th>
</tr>
</thead>
<tbody>
<tr>
<td>P-value:</td>
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<tr>
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<tr>
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<td>0.001375</td>
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<tr>
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standard error of difference = 0.001

Average area of axons

Alpha: 0.05

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standard error of difference = 11.667
### Data

**Average circularity of axons**

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Standard error of difference = 0.026

**Number of axons per fiber**

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Standard error of difference = 132.822

Alpha: 0.05
Conclusions

• Cisplatin did not have a significant effect on the nerve morphology of the musk shrew
• The 3 day injection period showed no significant effect
Limitations

• Nerve samples may have been damaged during removal

• Sample size may have contributed to an inaccurate view of the data
Future directions

• Investigate pharmacological methods of protection

• Study the change in function (e.g., nociception)
Acknowledgments and References

• Mark Krotec M.S.
• Eric Dunkerley
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• http://www.ncbi.nlm.nih.gov/pubmed/24430885
• http://www.autonomicneuroscience.com/article/S1566-0702%2812%2900004-5/abstract
• http://www.researchgate.net/publication/13563743_Brainstem_origin_of_the_efferent_components_of_the_cervical_vagus_nerve_in_the_house_musk_shrew_Suncus_murinus