Rodent Models of Spinal Cord Injury

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To put things in perspective:

- 291,000 people in the United States have a spinal cord injury (SCI)
- There are 17,730 new SCI cases per year
- 80% are males
- Lifetime costs can exceed $2M
- Personal costs to families
- >59% of SCI cases are at the cervical level
  - can result in respiratory motor insufficiency leading to dependence on mechanical ventilators
  - diminished quality of life

National SCI Statistical Center, 2019
State of the science:
• A majority of the pre-clinical animal SCI research utilizes rodents
• Function or outcome measure usually dictates the models utilized
  – Examples:
    • forelimb or hindlimb function
    • pain
    • autonomic dysreflexia
    • bladder or bowel movements
• Heterogeneity of the injury (level, injury type, time after initial trauma)
State of the science:

- injury
- treatment
  - neurotrophic factors
  - ECM modification
  - cell intrinsic systems
  - stem cell relay systems
  - rehabilitation
  - stimulation paradigms
    - sprouting
    - synaptic strengthening
    - plasticity
    - neuroprotection
- outcomes
  - behavior
  - anatomy
  - survival
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**Cervical spinal cord injury**

effective strategies

- neurotrophic factors
- ECM modification
- stem cell relay systems
- rehabilitation
- stimulation paradigms*
  - sprouting
  - synaptic strengthening
  - plasticity

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*Christopher Reeve, 2003

National SCI Statistical Center, 2019
Goal: To effectively model cervical SCI and impaired breathing in order to develop effective therapeutic strategies to promote respiratory motor function

To accomplish this, we:
- Model chronic Injury
- Model Cervical Contusions
Mid-cervical spinal cord contusion causes robust deficits in respiratory parameters and pattern variability

Philippa M. Warren, Cara Campanaro, Frank J. Jacono, Warren J. Allain

Rapid and robust restoration of breathing long after spinal cord injury

Philippa M. Warren, Stephanie C. Steiger, Thomas E. Dick, Peter M. MacFarlane, Warren J. Allain, and Jerry Silver

Plasticity Induced Recovery of Breathing Occurs at Chronic Stages after Cervical Contusion

Philippa Mary Warren and Warren Joseph Allain

Published Online: 5 Feb 2019 | https://doi.org/ezproxy.uky.edu/10.1089/neu.2018.6186
Goal: To effectively model cervical SCI and impaired breathing in order to develop effective therapeutic strategies to promote respiratory motor function.

To accomplish this, we:
- Model chronic injury
- Model cervical contusions
- Consider human genetic diversity
Our experiments in the lab:

• inbred rodents
  – same sex, strain, developmental stage
• similar genetic backgrounds
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Reality:
- humans are diverse
- there may be *genetic predispositions or aversions* towards regeneration and plasticity
  - this can impact our experimental treatment strategies moving forward towards human application

Human genetic variance impacting regeneration and plasticity
“humanized” mouse models: mice with relevant human genes
Breakthroughs in SCI research using rodents

To name just a few:

- Robust regeneration
- Plasticity
- Functional stimulation
- Impact of the gut microbiome
- Secondary complications
Rodents in SCI research:
• Already the preferred model for SCI research
• Breakthroughs made which have led directly to human studies (theophylline)
• Genetic tools are readily available

Canines in SCI research:
• Naturally SCI models already exist
• Breakthroughs in canine SCI research applicable to both dogs and humans
• Spinal cord is accessible in dogs vs. microsurgery in rodents
THANK YOU