Nutrition, Gut Microbiome, and Cardiometabolic Health in Individuals with Spinal Cord Injury

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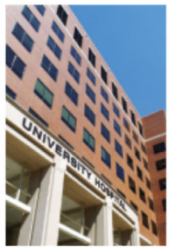
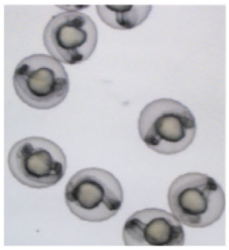
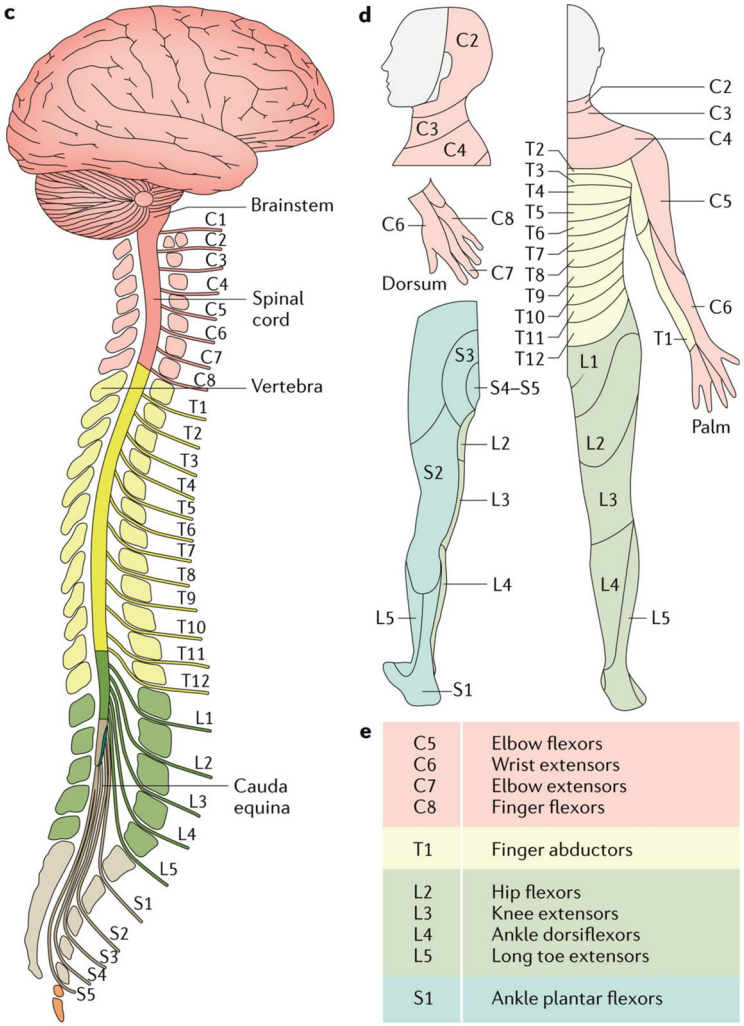







What is a Spinal Cord Injury (SCI)?

- Damage to the spinal cord, which is a bundle of nerves and cells responsible for sending and receiving signals from the brain to and from the rest of the body
- SCI hinders the body's ability to send and receive neurological signals, which impacts sensation, movement, and bodily function
- Levels of injury: section of the spinal cord damaged
- Severeness of injury:
  - Complete = no sensory or motor function preserved in affected areas
  - Incomplete = partial sensory and motor function; some messages can be transmitted to and from brain to rest of body



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SCI: Incidence, Causes, Demographics

- 17,900 new SCI cases each year in the U.S.
- Lifetime cost ~1-5 million direct health care cost per person.

National Spinal Cord Injury Statistical Center (NSCISC)

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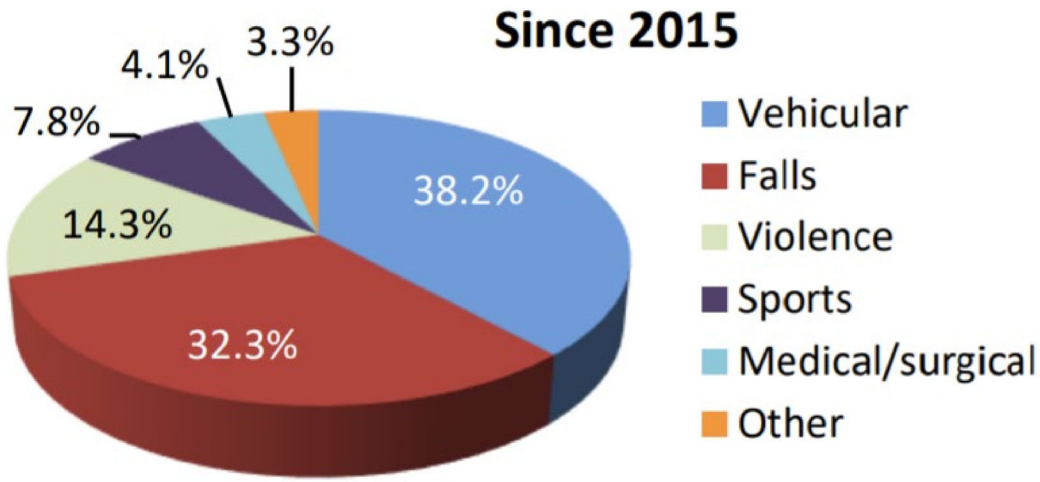

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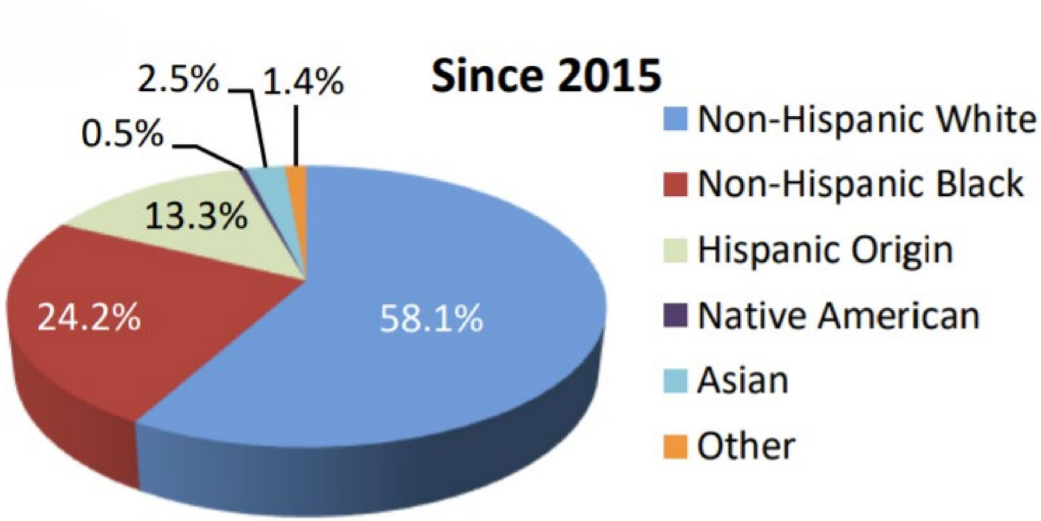

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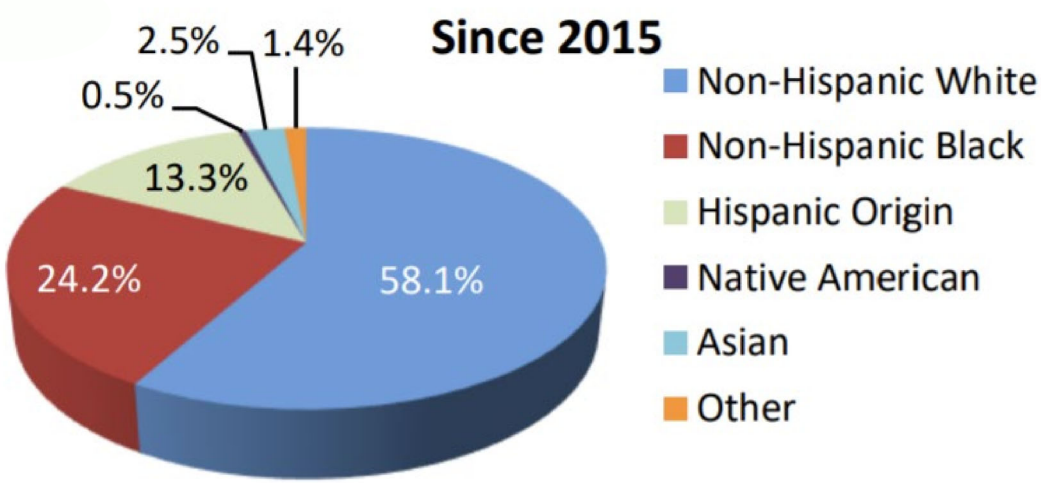

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Impact of SCI on the Human Body

Impaired physical function

Sensory Loss

Secondary Conditions:

Muscle Atrophy and Adiposity

Glucose and lipid disorders

Gut dysbiosis

Many more conditions (autonomic dysreflexia, kidney diseases, pressure ulcers, infections)

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Secondary Conditions:
a condition that is causally related to a disabling condition (that is, occurs as the result of a primary disabling condition)

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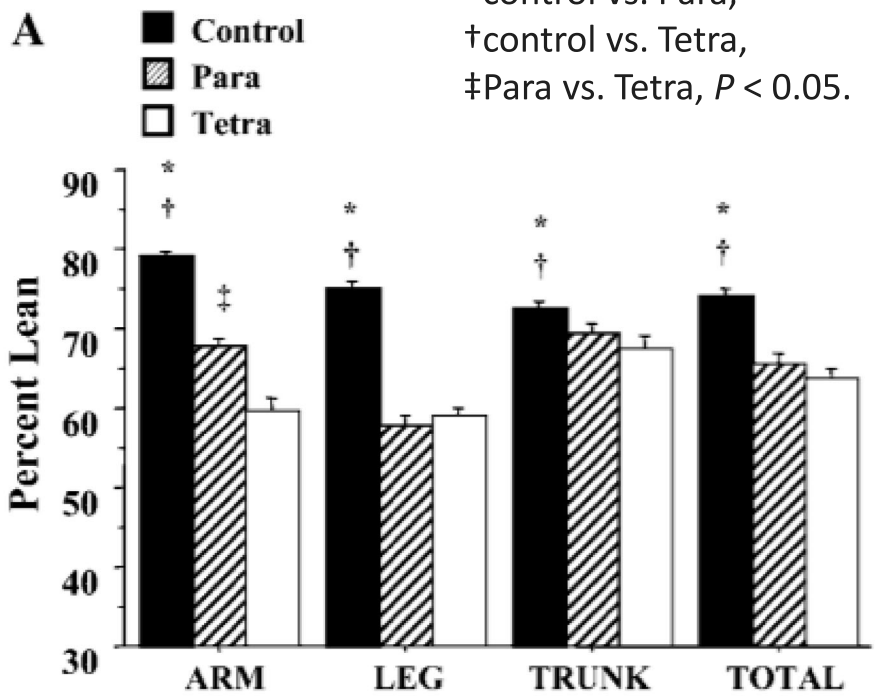

*control vs. Para,
†control vs. Tetra,
‡Para vs. Tetra, $P < 0.05$.

Spungen AM. J Appl Physiol 2003 (95)

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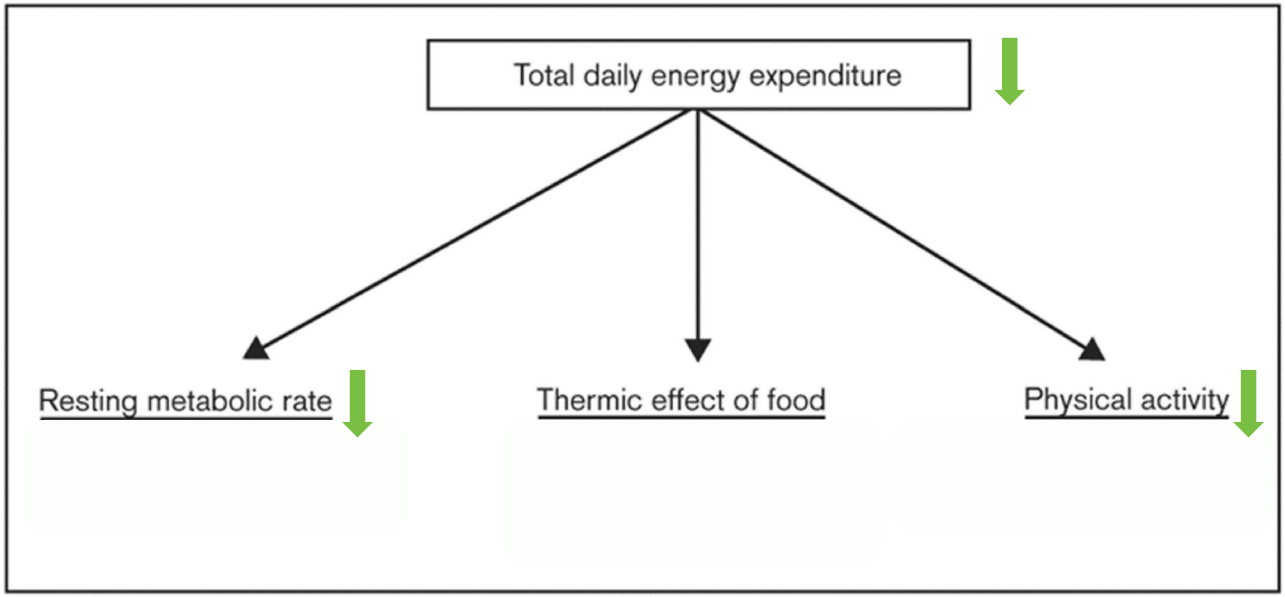

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Jones LM, et al, Archive PM&R, 2003

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Green Line: SCI

Black line: Controls

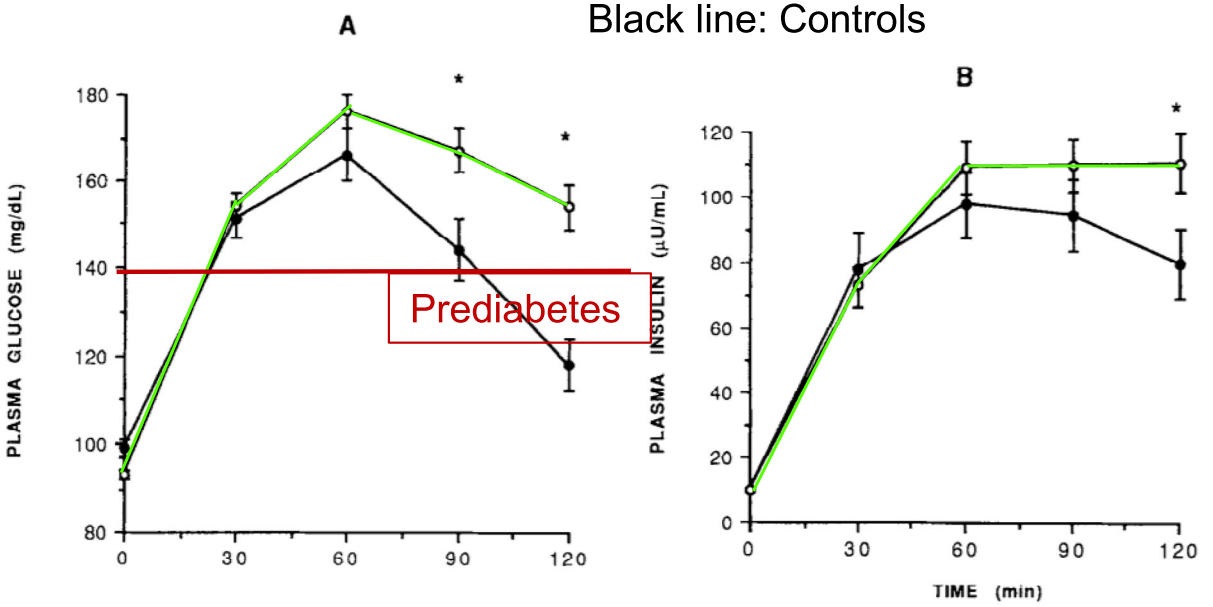

Fig 1. Mean plasma (A) glucose and (B) insulin values ± SEM during a 2-hour OGTT performed on 100 subjects with SCI (O) and 50 control subjects (●). *$P < .05$.

Bauman WA, et al. Metabolism, 1994 (143)

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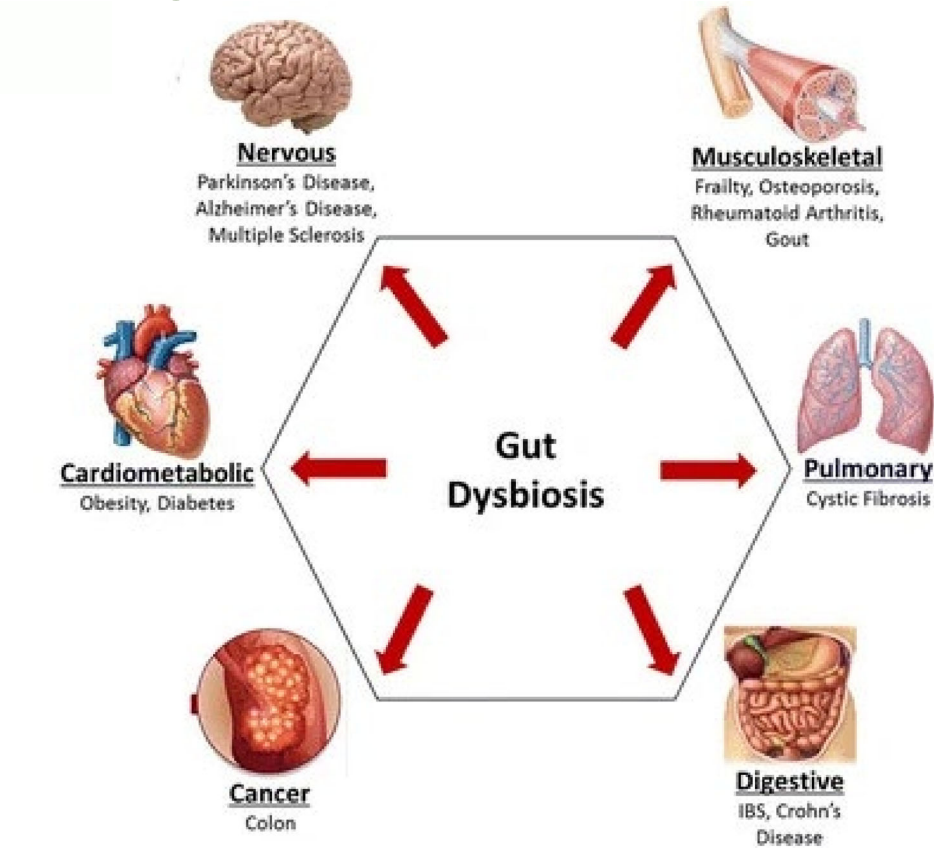

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Buford TW. Microbiome. 2017(5)

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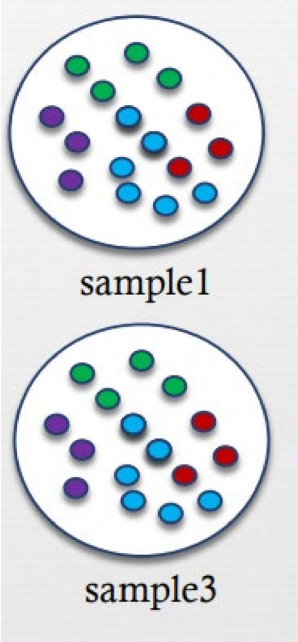
Alpha diversity: Measurement of Microbiome Diversity within a Sample

- Richness: a measure of number of species present in a sample.
- Evenness: a measure of relative abundance of different species that make up the richness in that area

Impact of SCI on the Human Body



Equally rich and even

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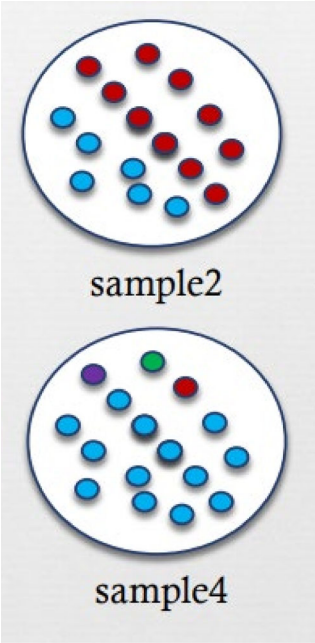

Sample 4 is richer but less even

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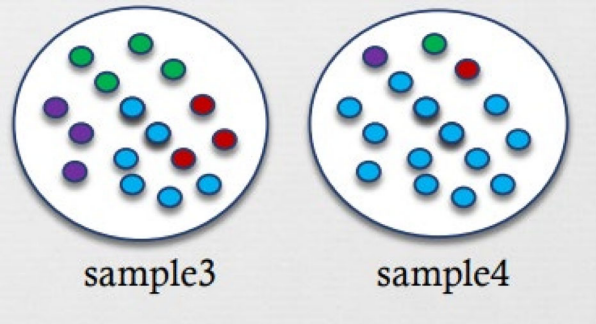

Equally rich

Sample 4 is less even

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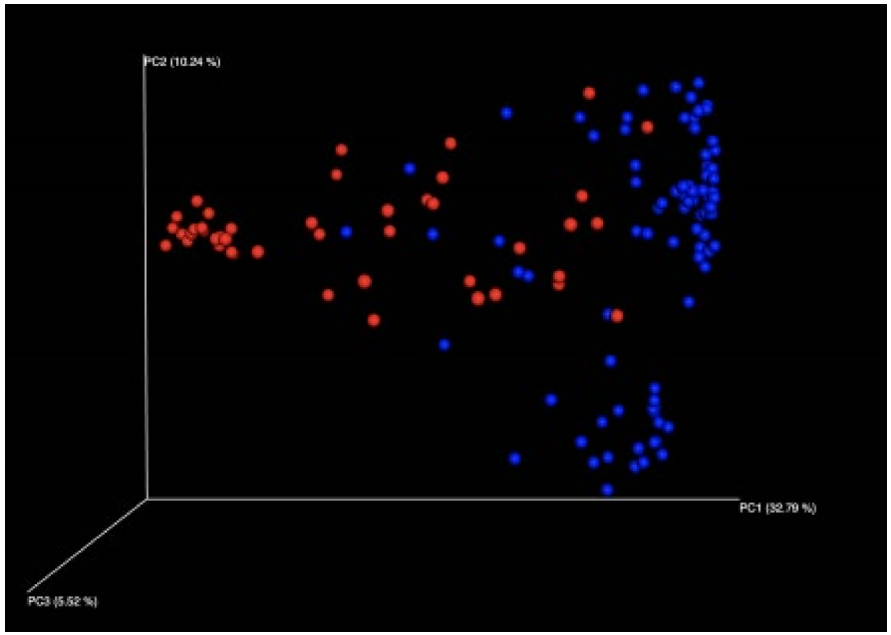
Impact of SCI on the Human Body

Beta-diversity: Measure of the Microbiome Diversity between Samples

- When more than two samples are used, the beta diversity is calculated for every pair of samples to generate a distance/dissimilarity matrix
- Distances between groups can be compared
- Allows visualization of group distances



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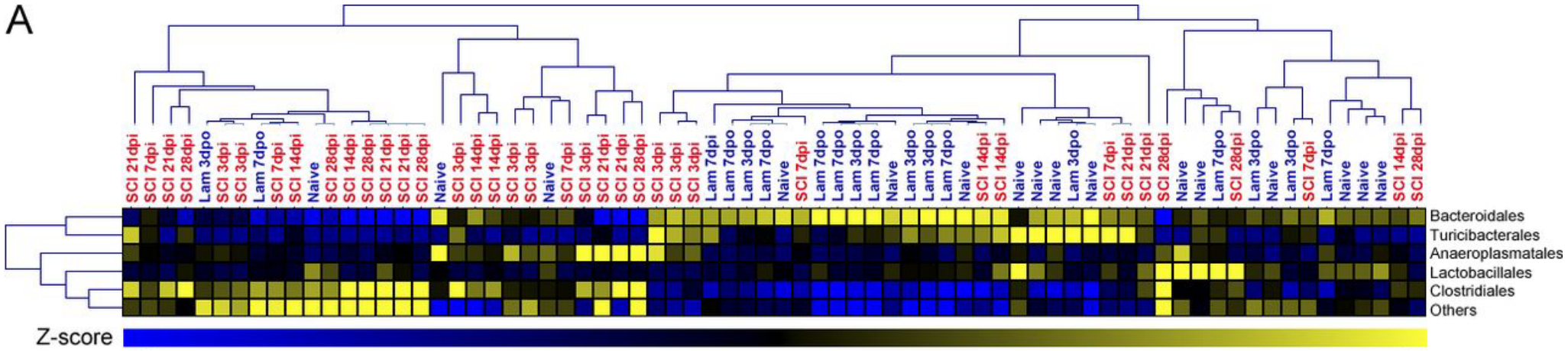
Acute SCI Induces Gut Dysbiosis and Bacteria Translocation

Mice, T9 contusion spinal injury (3, 7, 17, 28 days after injury, acute phase)
vs.
Sham control



Kigerl KA, et al. J Exp Med 2016(12)

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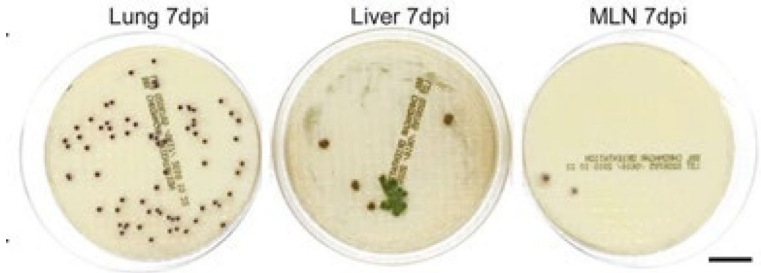
Acute SCI Induces Gut Dysbiosis and Bacteria Translocation

	Naive	1dpi	3dpi	7dpi
Blood	0% (0/4)	0% (0/4)	0% (0/4)	*25% (1/4)*
Lung	0% (0/4)	0% (0/4)	*25% (1/4)*	*100% (4/4)***
Liver	0% (0/4)	0% (0/4)	0% (0/4)	*75% (3/4)***
Spleen	0% (0/4)	0% (0/4)	0% (0/4)	*50% (2/4)**
MLNs	0% (0/4)	0% (0/4)	0% (0/4)	*75% (3/4)***

**p<0.05, **p<0.01*



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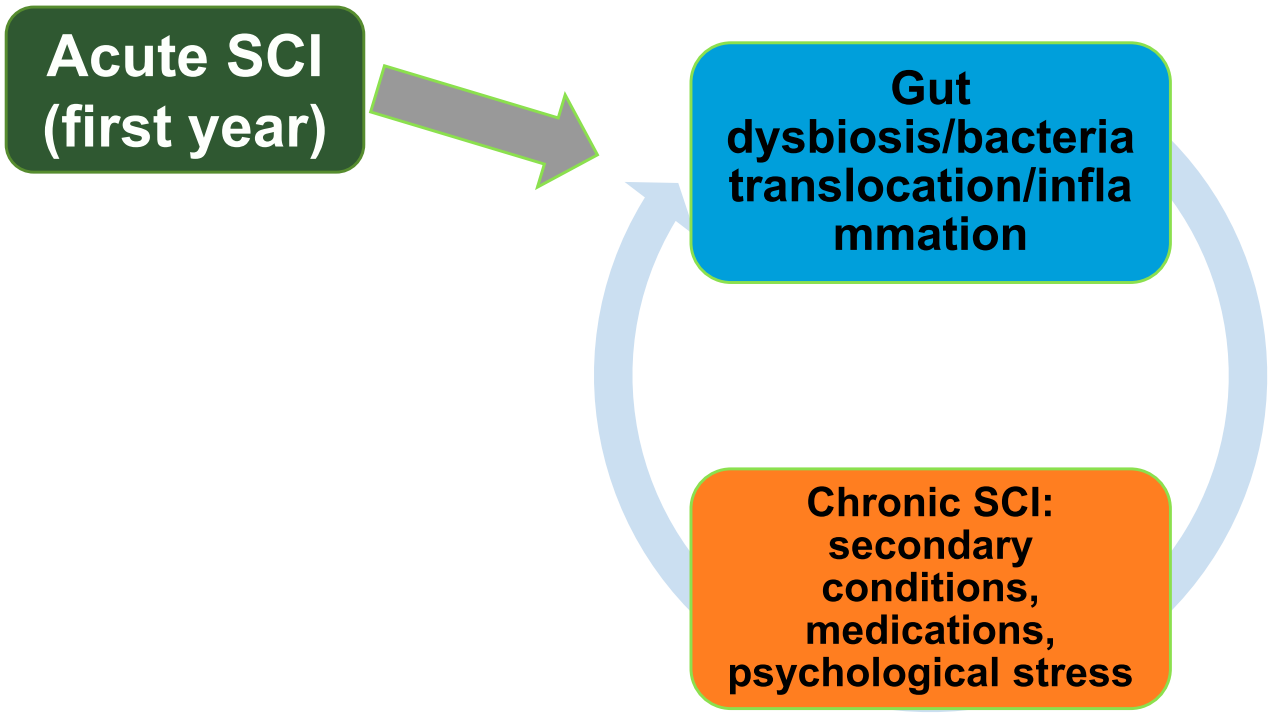
SCI Creates A Vicious Cycle of Gut Dysbiosis



Does Gut Microbiome Deteriorate Overtime after SCI?

Group	Controls	A-SCI	C-SCI
Total, n	25	7	25
Age, y	42 ± 13	36 ± 12	46 ± 13
Sex (Female/Male)	9F/16M	2F/5M	6F/19M
Level of Injury[$], n	N/A	C: 5 T: 2	C: 6 T: 17 L: 2
Severity of Injury, n	N/A	AIS A: 2 AIS B: 1 AIS C: 3 AIS D: 1	AIS A: 17 AIS B: 2 AIS C: 2 AIS D: 4
Time of stool collection post-injury	N/A	7 days; min 4, max 11	18 years; min 3, max 53
Antibiotics Use	0	n=6	0

Li J, et al. J Spinal Cord Medicine, 2020

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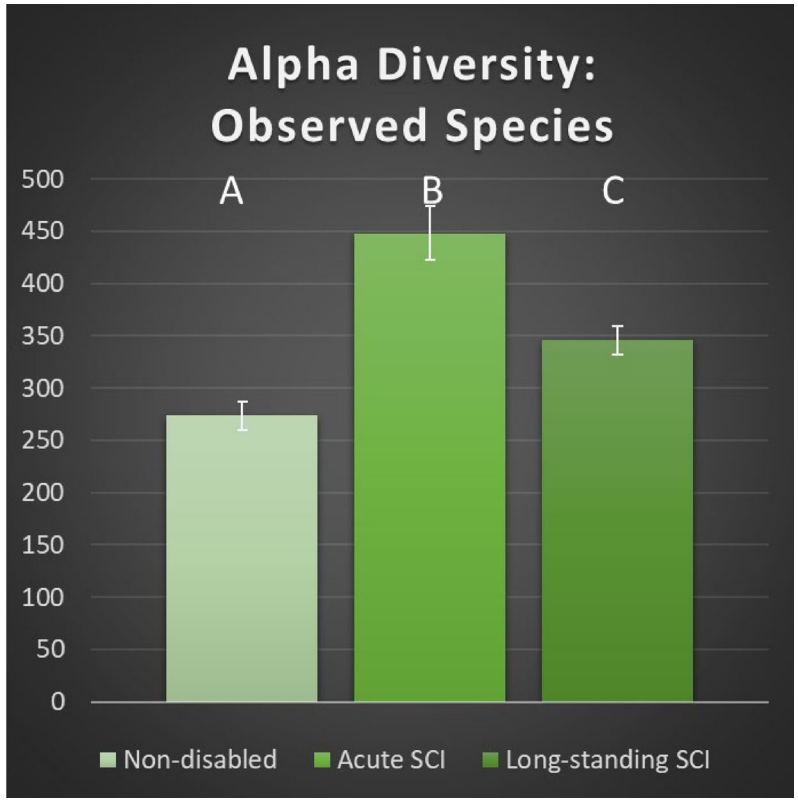
Li J, et al. J Spinal Cord Medicine, 2020

Gut Microbiome Differed among the Groups



Li J, et al. J Spinal Cord Medicine, 2020

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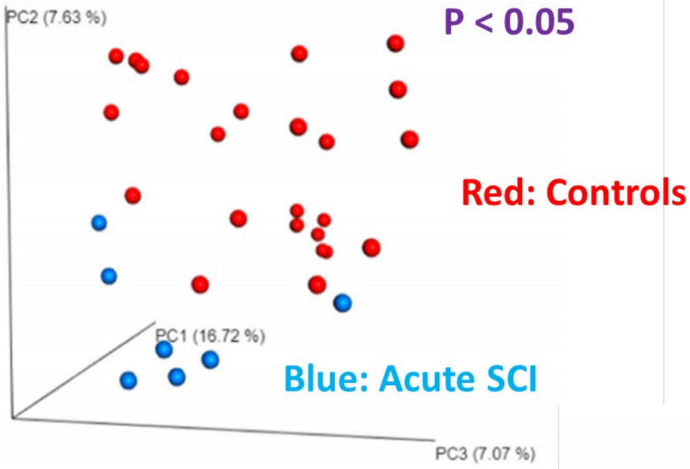

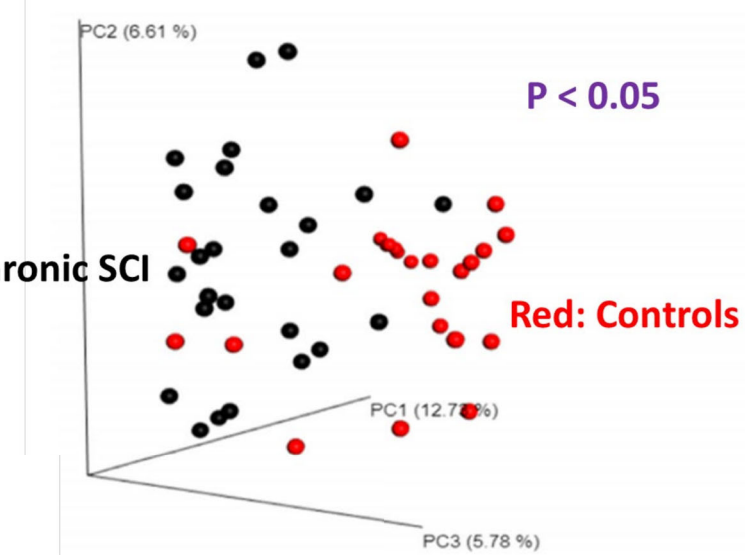

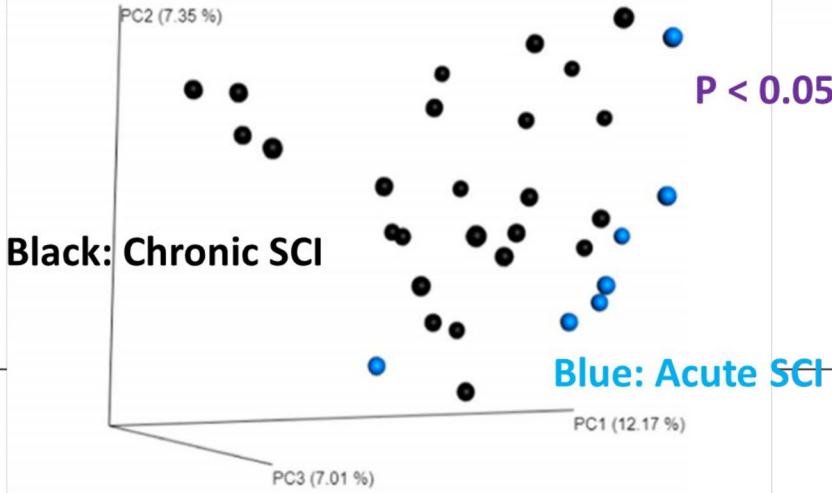

Li J, et al. J Spinal Cord Medicine, 2020

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Changes in gut microbiome may be unfavorable:

- Compared to the control group, microbiome composition in the SCI groups share features linked to metabolic syndrome, inflammation-related bowel disorders, depressive disorders, or antibiotics use.
- Compared to A-SCI and control groups, individuals with C-SCI share features linked to physical inactivity.

SCI Negatively Affects Many Organ Systems

Impaired physical function

Sensory Loss

Secondary Conditions:

Muscle Atrophy and Adiposity

Glucose and lipid disorders

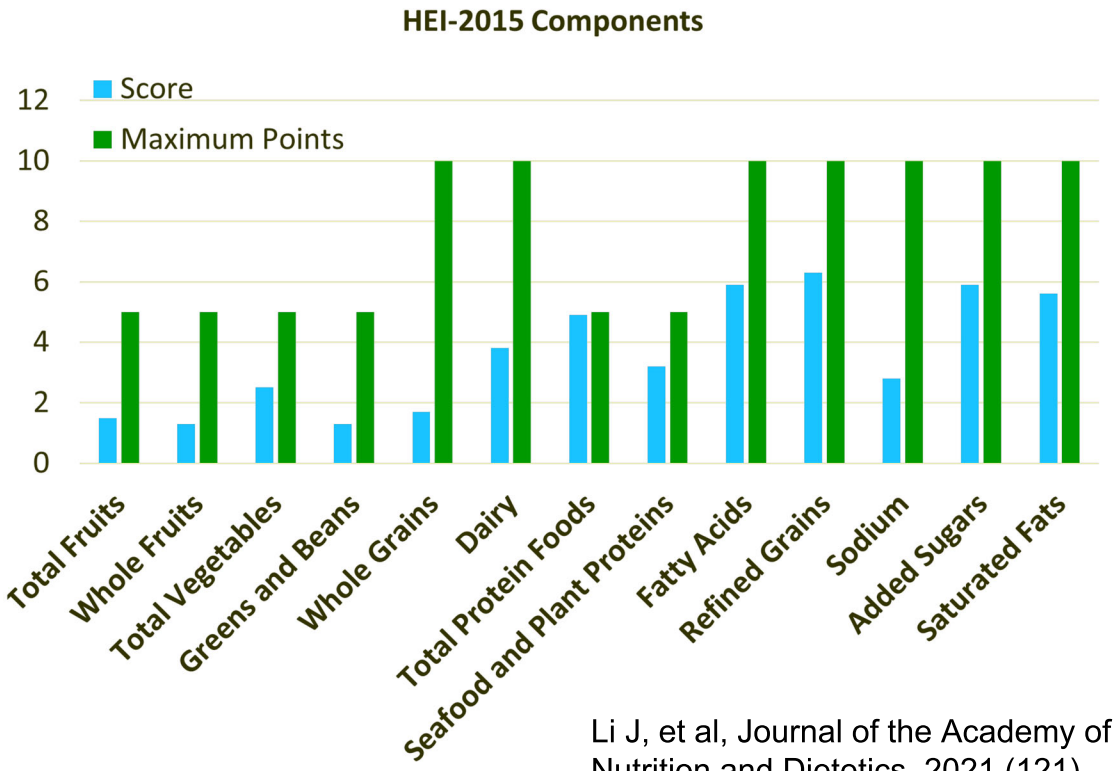
Gut dysbiosis

Many more conditions (autonomic dysreflexia, kidney diseases, pressure ulcers, infections)

Individuals with SCI Consumes Poor Diets

Average Healthy Eating Index: 47

Healthy Eating Index of the U.S. Adults: 59



Li J, et al, Journal of the Academy of Nutrition and Dietetics, 2021 (121)

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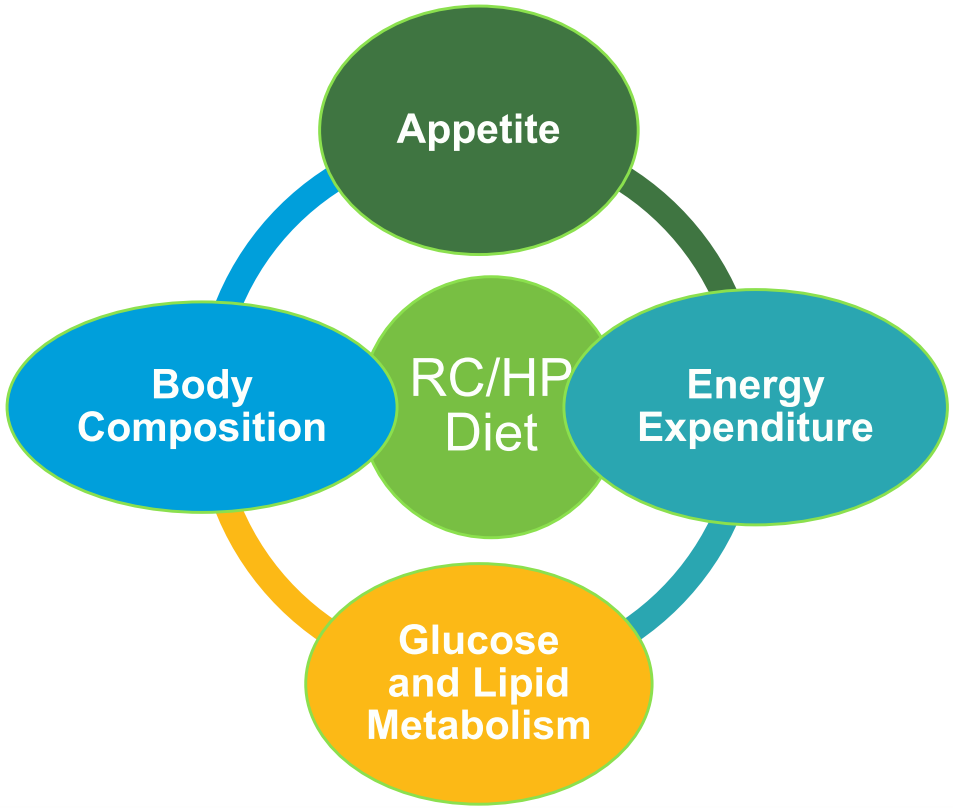
Could a Reduced-Carbohydrate/High-Protein Diet (with Healthy Components) Benefit Individuals with SCI?



Leidy H. Mo Med. 2014 (111)

Study Design

- **8 week, randomized controlled parallel study**

- **RC-HP Diet:**
  - ❑ Isocaloric (30% Protein; 30% Fat, 40% Carbohydrate)
  - ❑ Focuses on healthy components: whole grains, lean meat, fruits and vegetables, etc.
  - ❑ Meals delivered to participants weekly

- **Control group:** continue with their regular diets.

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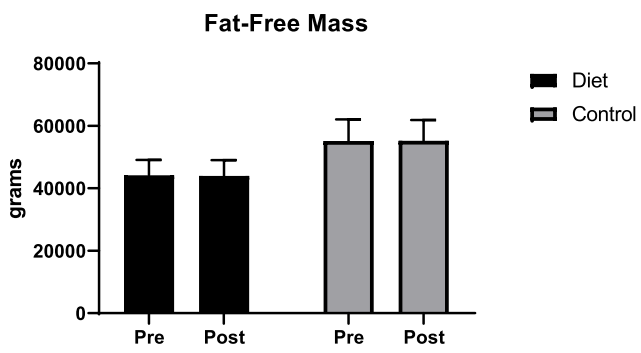
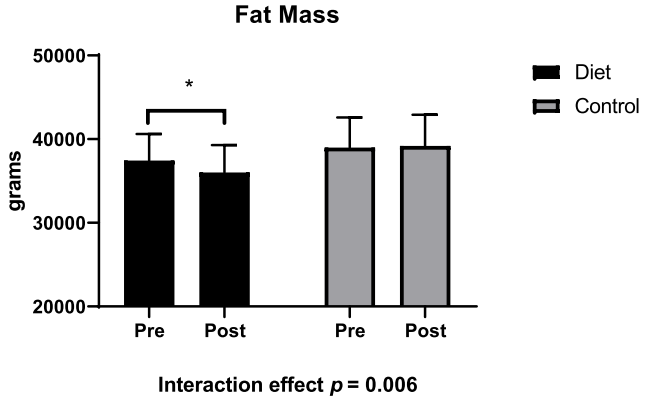
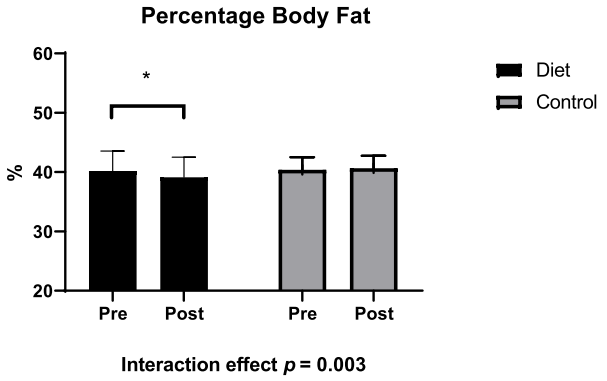
Eligibility:

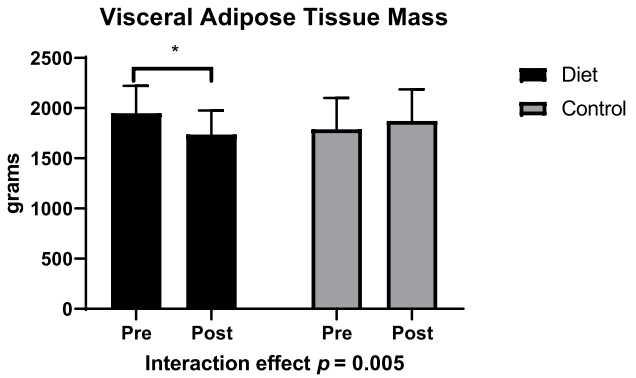
1) 18 to 65 years;
2) traumatic SCI at the cervical, thoracic, or lumbar level (C5-L2) classified as AIS A, B, C, or D;
3) Insulin resistant or impaired glucose tolerance
4) No antibiotics within 4 weeks prior to study
5) Not previously consuming a high-protein diet
6) No pressure ulcer

Results: RC/HP Diet Improved Body Composition









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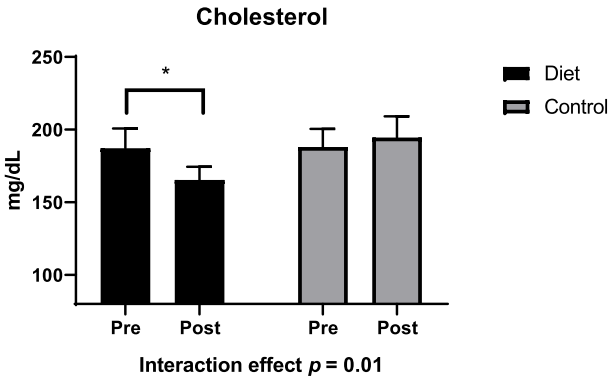
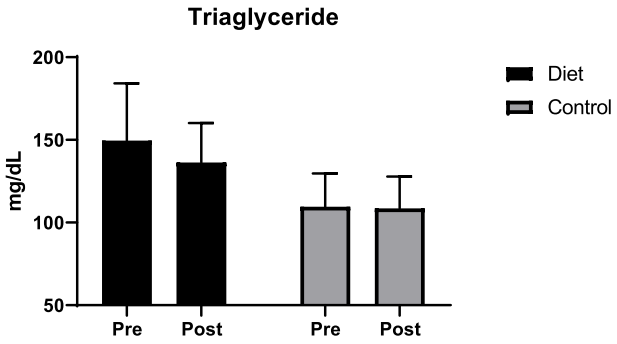
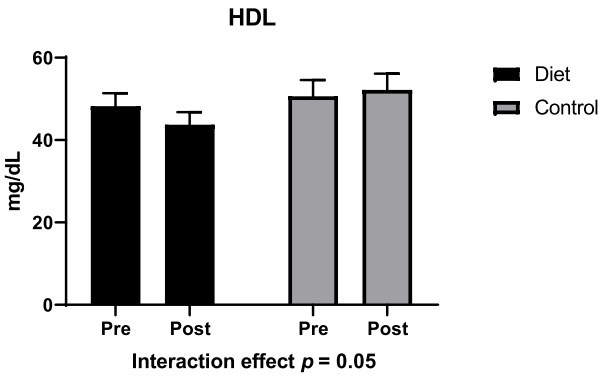
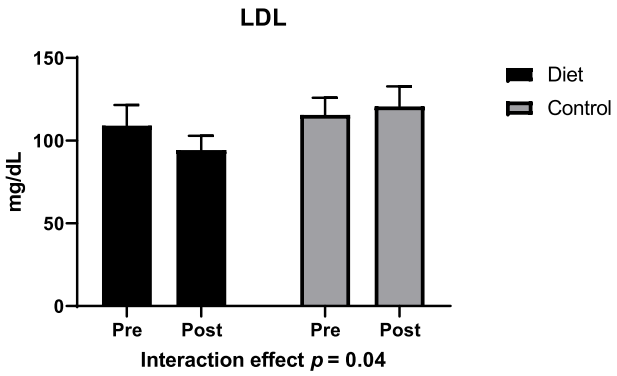
Results: RC/HP Diet improved Blood Lipid Profile









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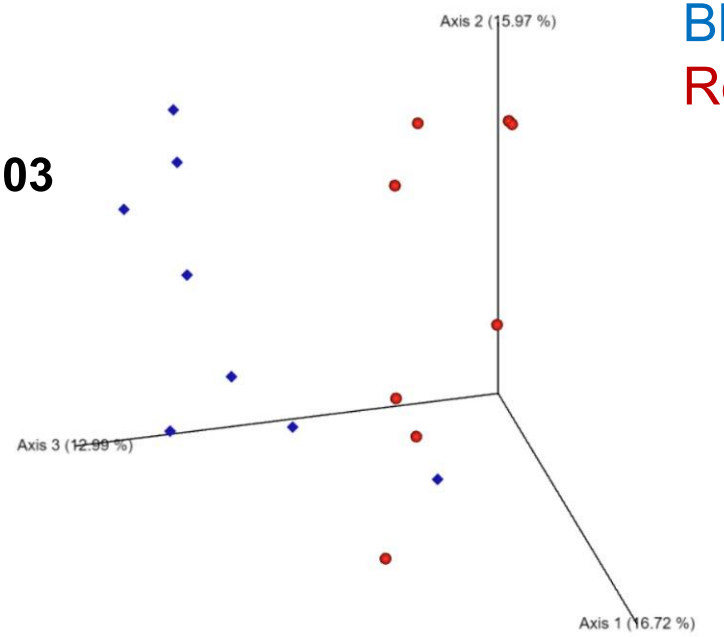
Results: Gut Microbiome Changed in Response to the RC/HP Diet

Alpha Diversity	**Diet**			**Control**			**P (interaction)**
	Pre	Post	P(pre and post)	Pre	Post	P (pre and post)	
OTU (richness)	**105.4 ± 38.8**	**78.3 ± 24.2**	**0.03**	101.1 ± 55.6	95.6 ± 51.1	0.76	0.6
Pilou's evenness	0.63 ± 0.17	0.70 ± 0.07	0.74	0.71 ± 0.08	0.66 ± 0.11	0.28	0.4
Shannon (richness + eveness)	4.1 ± 1.0	4.3 ± 0.4	0.61	4.6 ± 0.9	4.3 ± 0.9	0.40	0.5

Results: Gut Microbiome Changed in Response to the RC/HP Diet

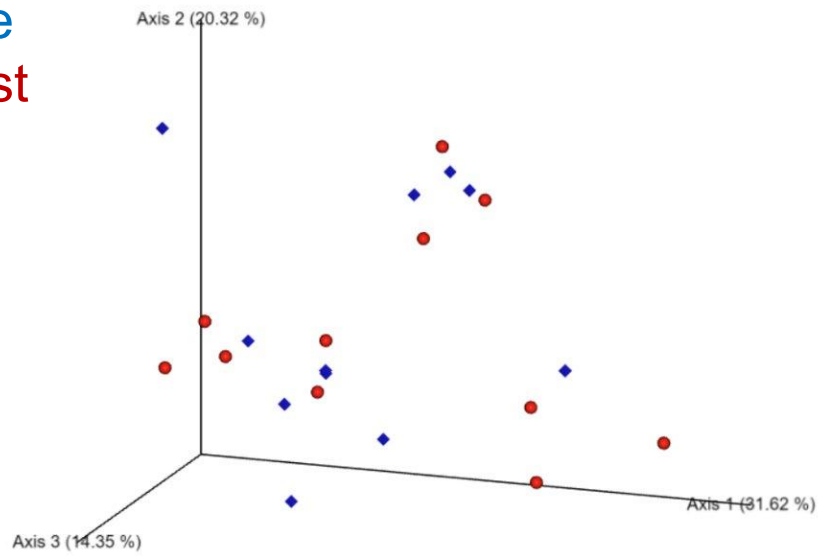
A. Diet group

P=0.03



Blue: Pre
Red: Post

B. Control group



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Results: Gut Microbiome Changed in Response to the RC/HP Diet

- Several microbial communities that are involved in fiber digestion and metabolism were increased [*Bacteroides thetaiotaomicron* (species), Coprococcus 3 (genus), and Fusicatenibacter (genus)]
  - ❑ Community stability (providing fuels to other beneficial bacteria)
  - ❑ Alleviate intestinal inflammation
  - ❑ Maintain gut barrier integrity
  - ❑ Improved bowel function (constipation)
- Several bacteria taxa implicated in inflammation, metabolic disorders, and cardiovascular diseases were reduced [Tyzzerella, Phascolarctobacterium, Clostridium.sensu.stricto 1]

Summary/Discussion

- Spinal cord injury may be associated with progressive deterioration of the gut microbiome

- A RC/HP diet with healthy dietary components may use adopted to improve metabolic health and gut microbiome composition
  - ❑ Limitation: macronutrient composition or healthy components?
  - ❑ If and the extent of microbiome-conferred benefits?
  - ❑ Long-term safety, generalization?

- Future directions:
  - ❑ Prebiotic/Probiotics supplementation
  - ❑ Dietary manipulations to improve other secondary health conditions (pressure ulcer, blood pressure, etc)

Study Participants

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- Ceren Yarar-Fisher, PT, PHD
- Erika Womack, PhD
- Amal Alharbi, MS, PT
- Marguerite Marquez (PT student)
- Miles Gregorian (med student)
- Sarah Taylor (pre-med undergrad)
- Zoe Evans (undergrad)

Other faculty and staff

- Stephen Barnes, PhD
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UAB PROTEOMICS AND MASS SPECTROMETRY

Metabolomics

UAB THE UNIVERSITY OF ALABAMA AT BIRMINGHAM
Spinal Cord Injury Model System
School of Medicine

NATIONAL INSTITUTE ON DISABILITY, INDEPENDENT LIVING, AND REHABILITATION RESEARCH
NIDILRR

NIH
Eunice Kennedy Shriver National Institute of Child Health and Human Development

NIH National Institute of Nursing Research

Funding

- **90SI5019, The UAB Spinal Cord Injury Model Systems Grant NIDILRR Research PI:** Ceren Yarar-Fisher
- **1R01NR016443 NIH/NINR PI:** Ceren Yarar-Fisher
- **1K01HD087463 NIH/NCMRR PI:** Ceren Yarar-Fisher
- **KL2TR001419-01 UAB/CCTS PI:** Ceren Yarar-Fisher
- **90SFGE0018, NIDILRR PI:** Jia Li
- **Craig Neilsen Foundation Postdoctoral Fellowship**, Jia Li

Thank you and questions?