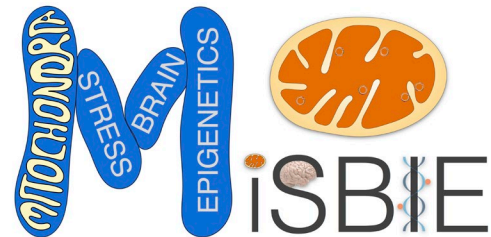


Allostatic load in people with mitochondrial diseases

Alex Junker

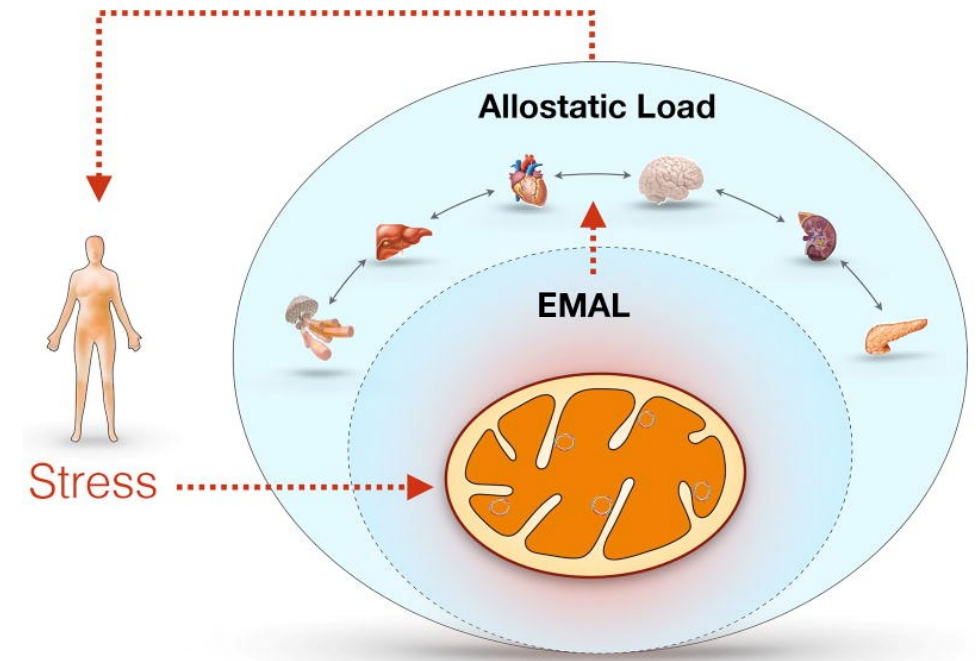
MiSBIE Symposium

December 12th, 2025



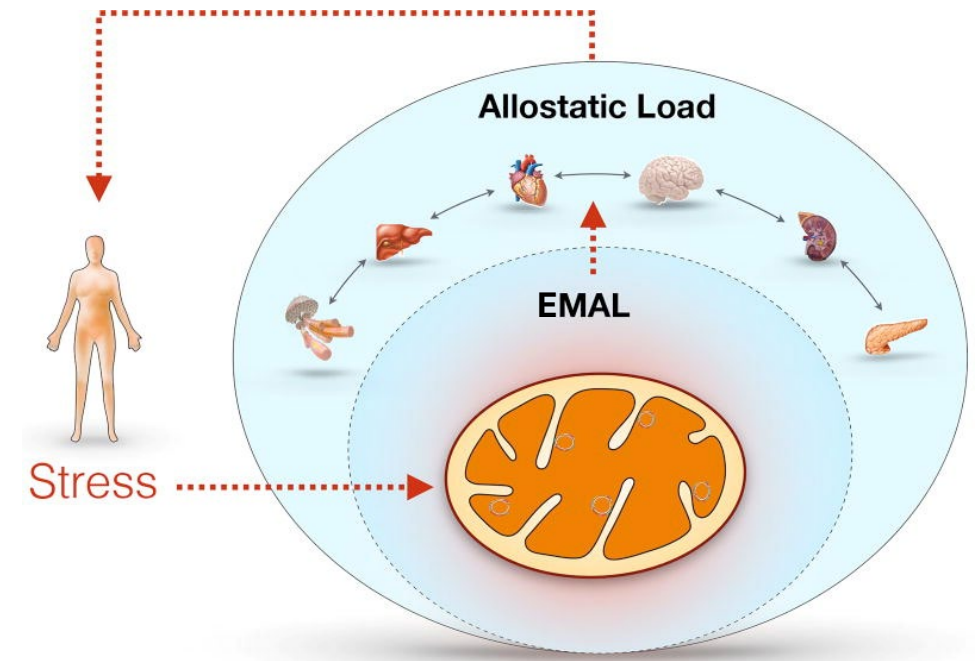
Psychological stress and allostatic load

- Psychological stress activates a systemic physiological response
 - Changes in cortisol, catecholamines, glucose, and blood pressure, among others^{1,2}



Psychological stress and allostatic load

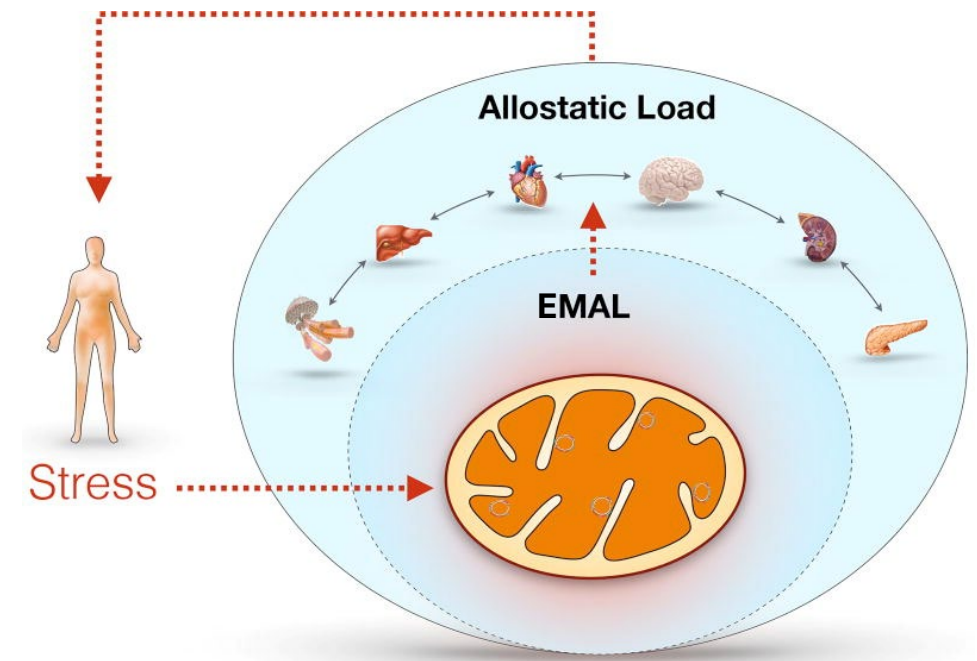
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1. Sapolsky, RM., Romero, LM., Muncz, AU. (2000).
2. McEwen, BS. (2017).
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Psychological stress and allostatic load

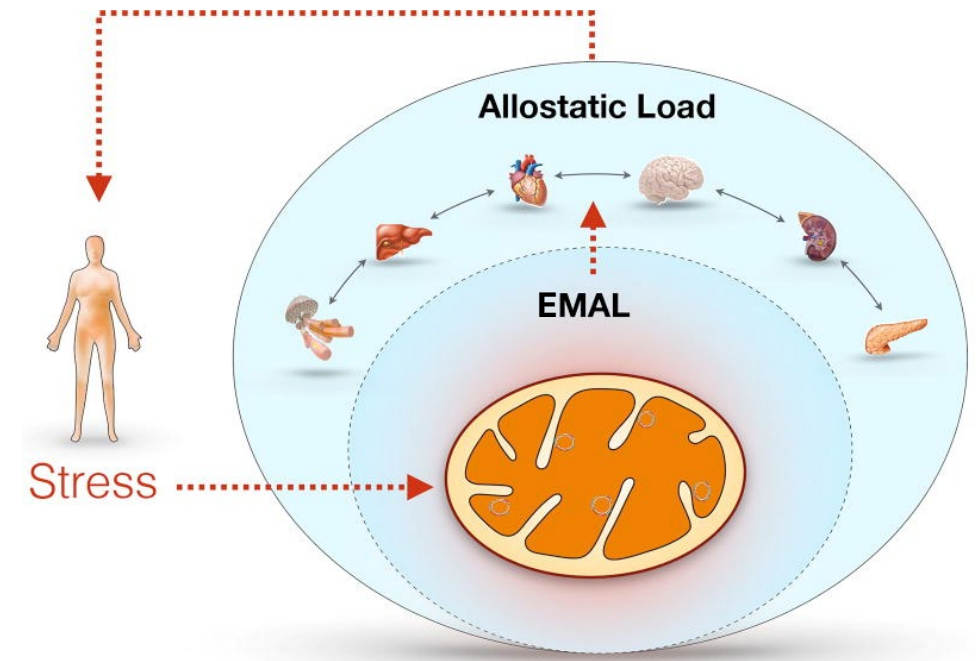
- Psychological stress activates a systemic physiological response
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- Chronic alteration of these parameters results in bodily 'wear and tear,' quantified as allostatic load (AL)^{3,4}
- High AL
 - depression⁵
 - neurodegenerative disease⁶
 - general physical and cognitive decline^{7,8}



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5. Gou Y., Cheng S., Kang M., Zhou R., Liu C., Liu Y., Wang B., Shi P., Zhang F. (2024).
6. Adedeji, DO., Holleman, J., Juster, RP., ... A., Sindi, S. (2023).
7. Gruenewald, TL., Seeman, TE., Karlamangla, AS., Sarkisian, CA. (2009).
8. D'Amico, D., Amestoy, ME., Fiocco, AJ. (2020).

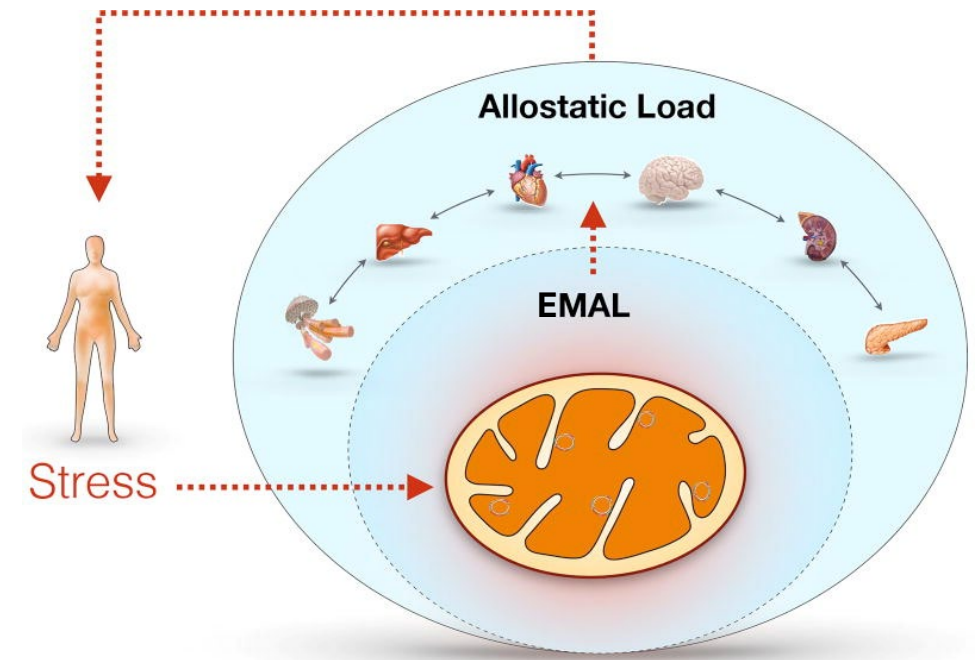
Allostatic load and energetic stress

- Stress responses require energy, mostly provided by mitochondrial oxidative phosphorylation⁹



Allostatic load and energetic stress

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- Genetic mitochondrial defects (MitoD) → energetic stress
 - Cells with MitoD use more energy, age faster, and have altered cytokine levels¹⁰
 - In mice, MitoD-induced energetic stress alters stress responses and triggers inflammation¹¹



9. Picard, M., McEwen, BS., Epel, E., Sandi, C. (2018).

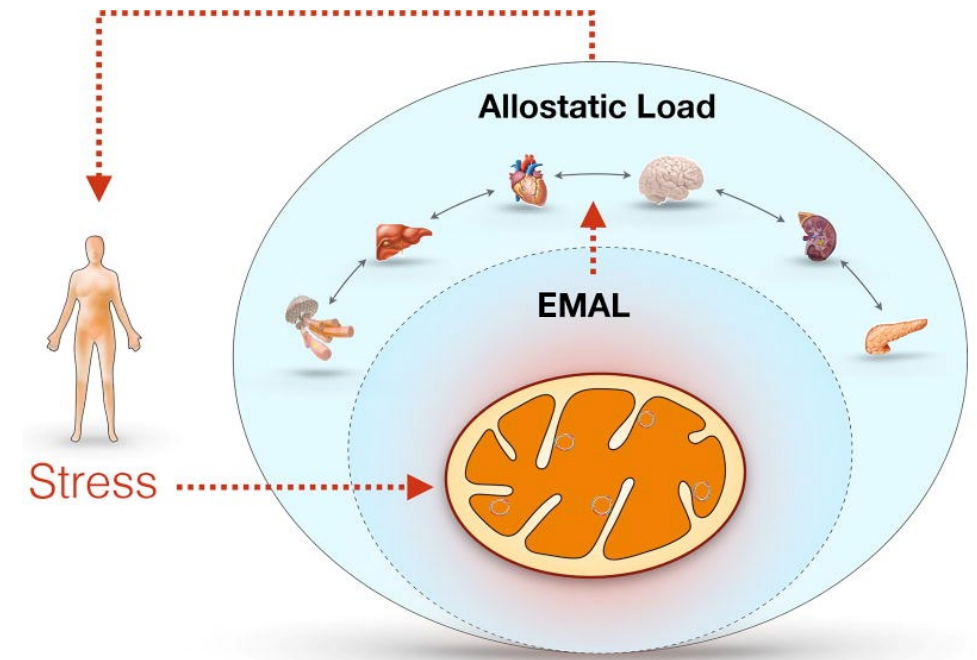
10. Bobba-Alves, N., Sturm, G., ... Picard, M. (2023).

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Allostatic load and energetic stress

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→ Energetic model of allostatic load (**EMAL**)¹²

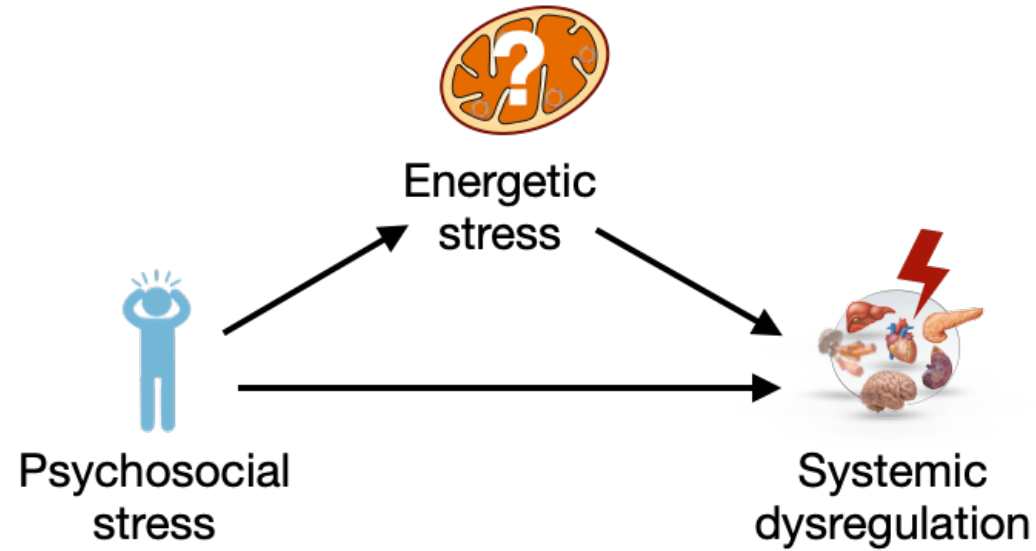


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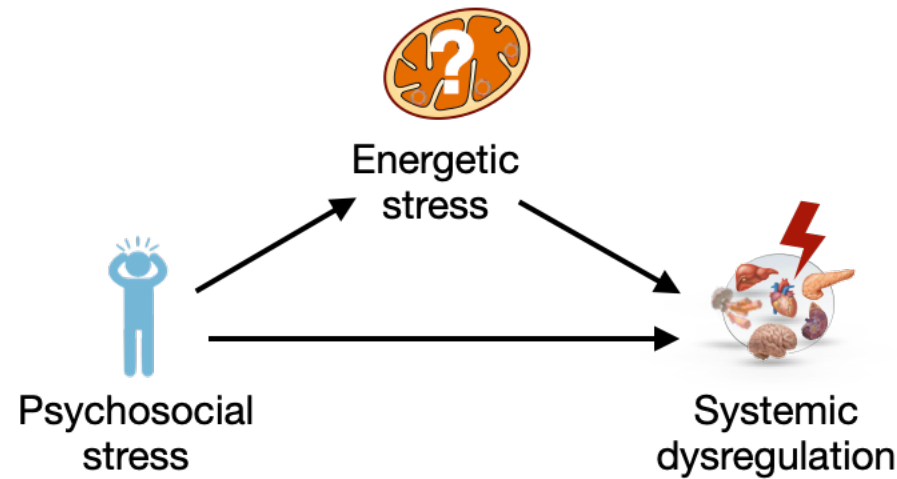
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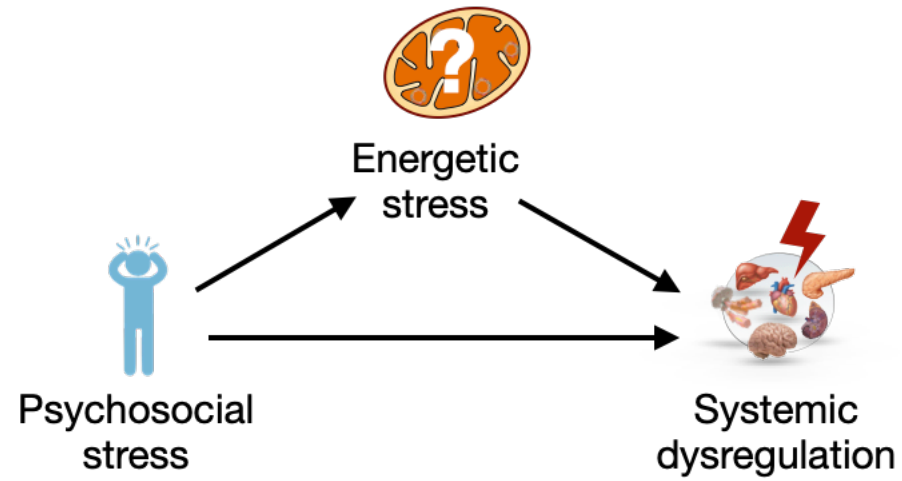
12. Bobba-Alves, N., Juster, RP., Picard, M. (2022).



Does the energetic stress of mitochondrial disease alter systemic dysregulation in humans?



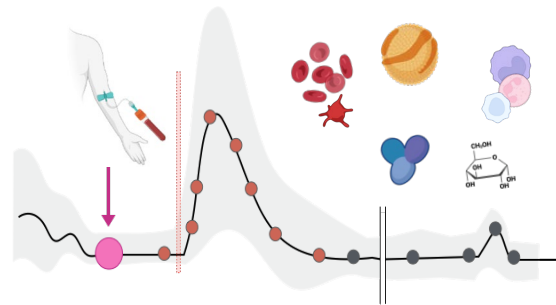
1. Is allostatic load higher in people with mitochondrial diseases?
2. Does it come from the same systems?
3. How/does it interact with psychological stress?



Control
n=69

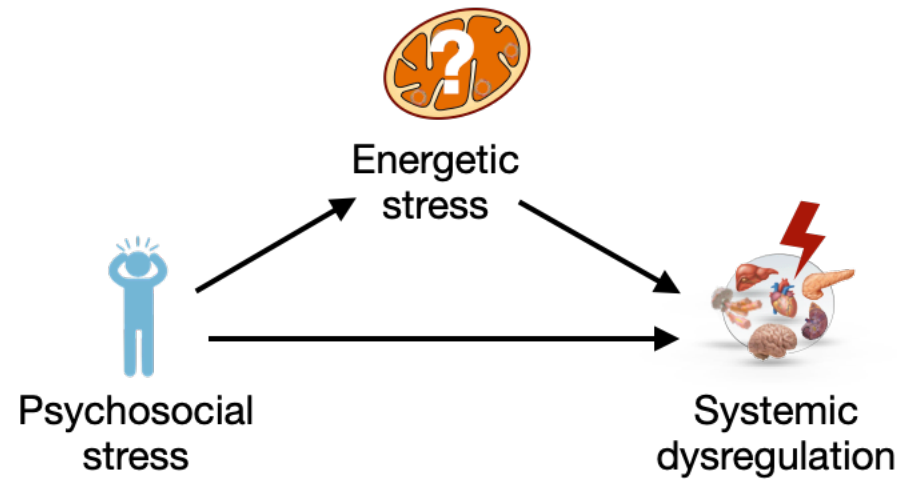
MitoD
n=36

Allostatic load



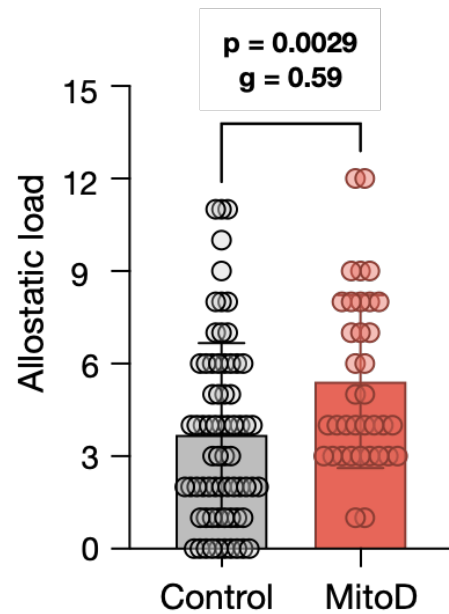
Questionnaires

- Lifetime stress exposure (Stress and Adversity Inventory, STRAIN)
- Exposure to chronic stress (Trier Inventory of Chronic Stress, TICS)
- Childhood maltreatment (Childhood Trauma Questionnaire, CTQ)

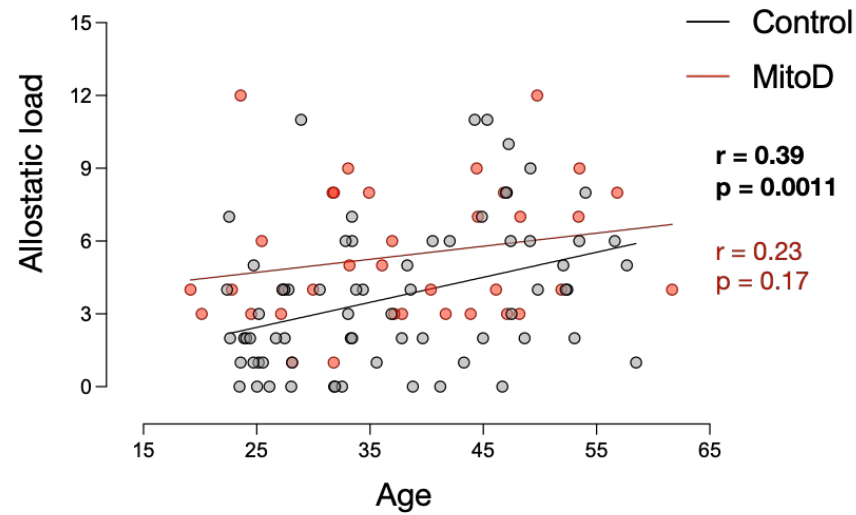
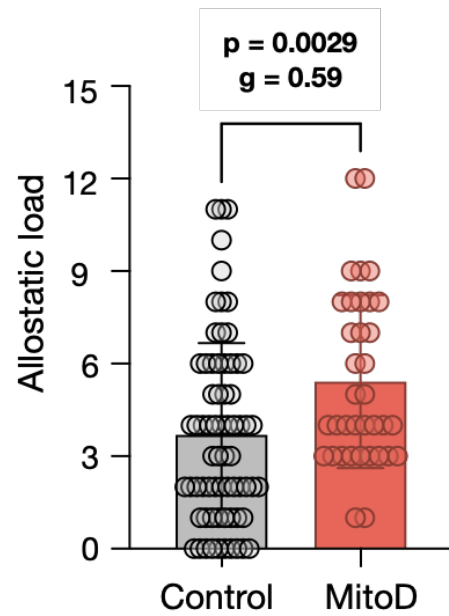


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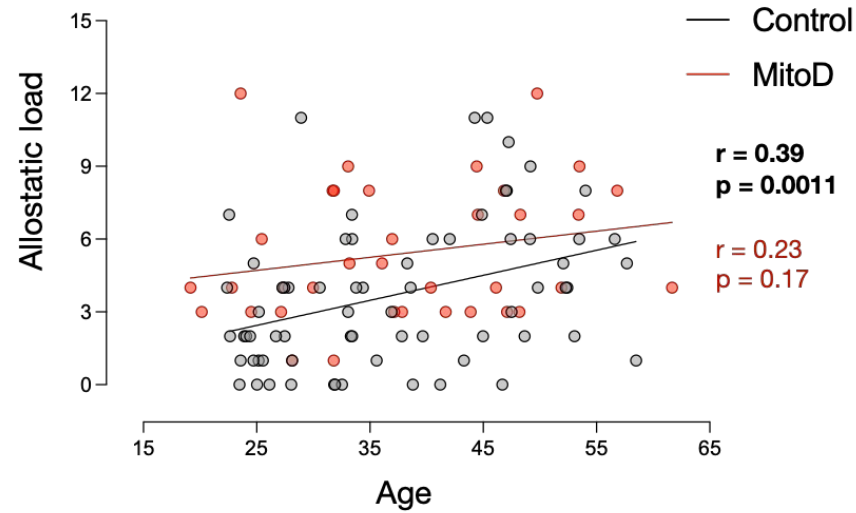
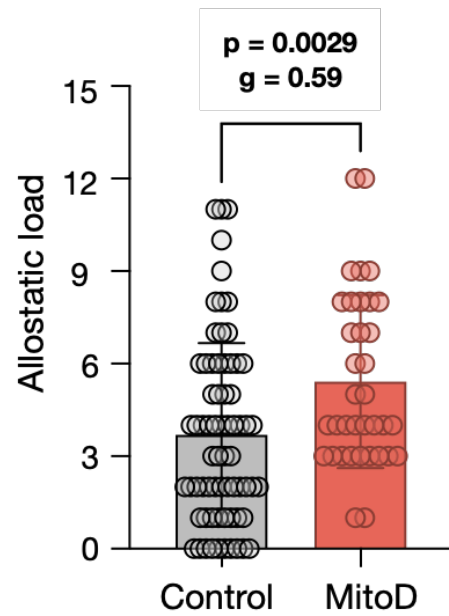
Allostatic load is higher in people with mitochondrial diseases



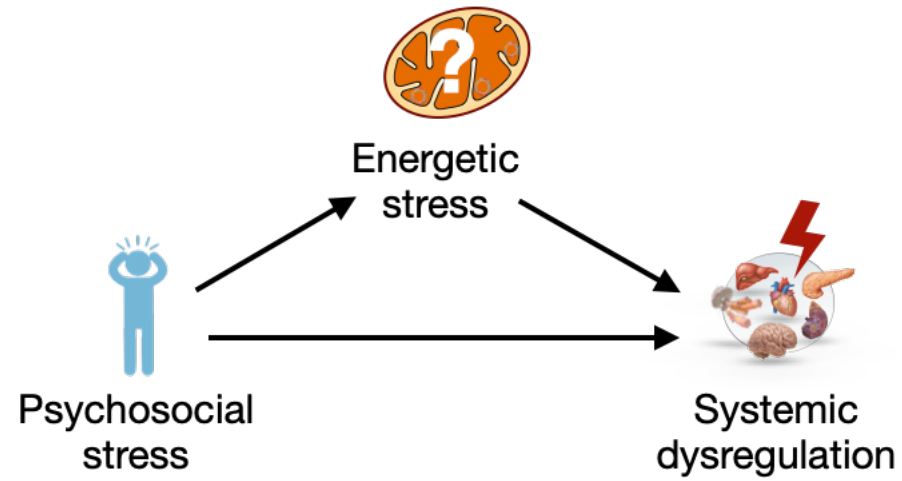
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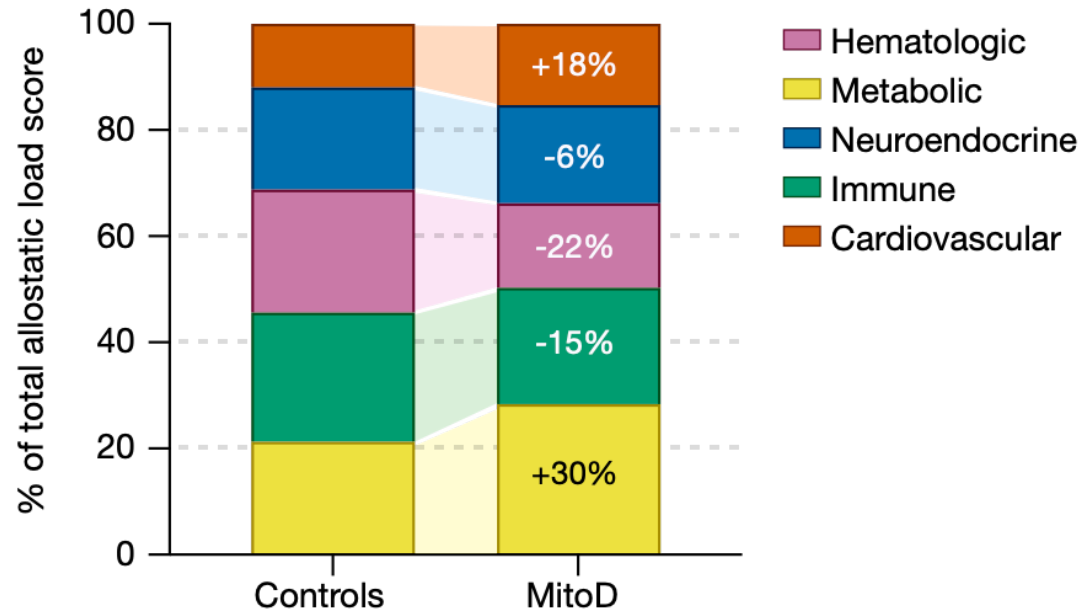


r=0.39
p=0.0008
r=0.23
p=0.21

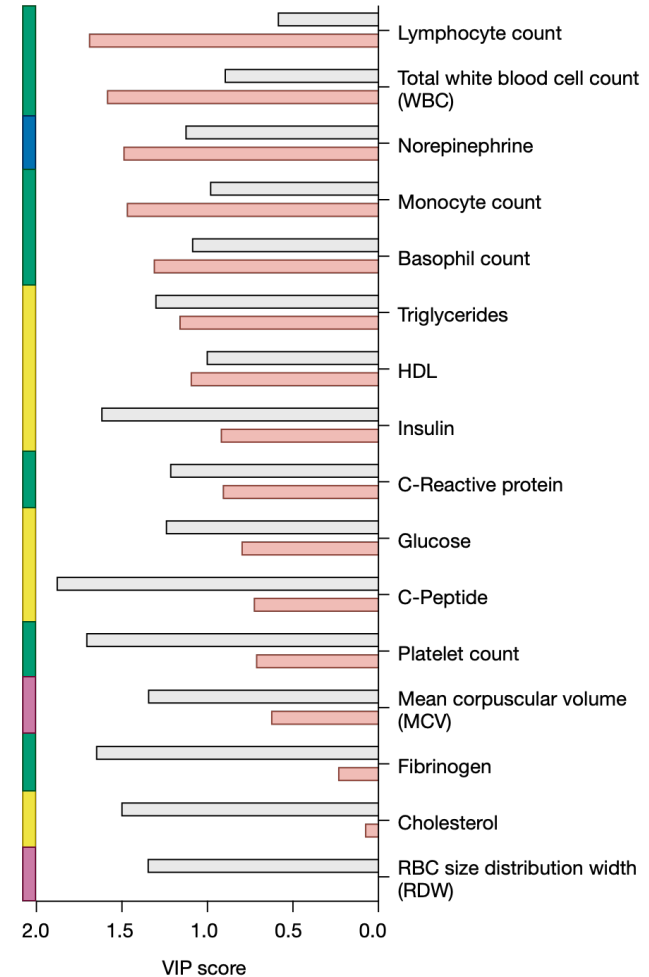
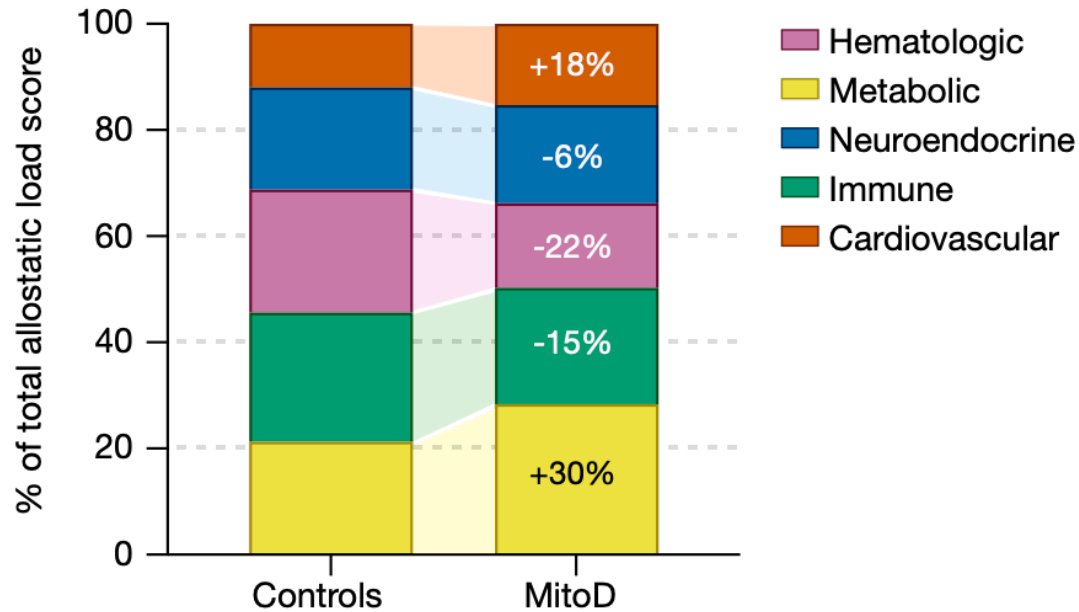


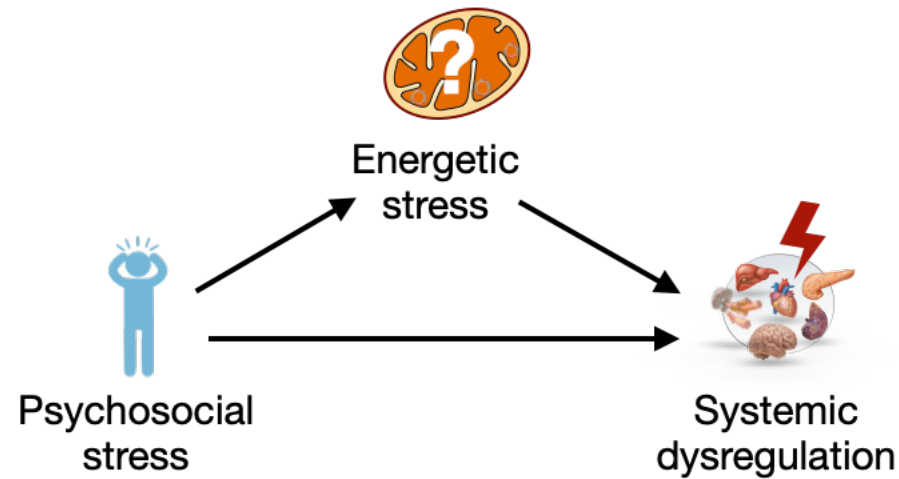
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System-specific dysregulation varies with mitochondrial disease



System-specific dysregulation varies with mitochondrial disease





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Measuring psychological stress

Stress and Adversity Inventory (STRAIN)

- Quantifies **lifetime stressor exposure**
- Participants say which stressors they have experienced
 - Domains: housing, finances, marital, legal, etc.
 - Aggregated into stressor count and feeling of threat

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 - Retrospective (previous year)
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 - Subscales: social tension, work discontent, chronic worrying, etc.

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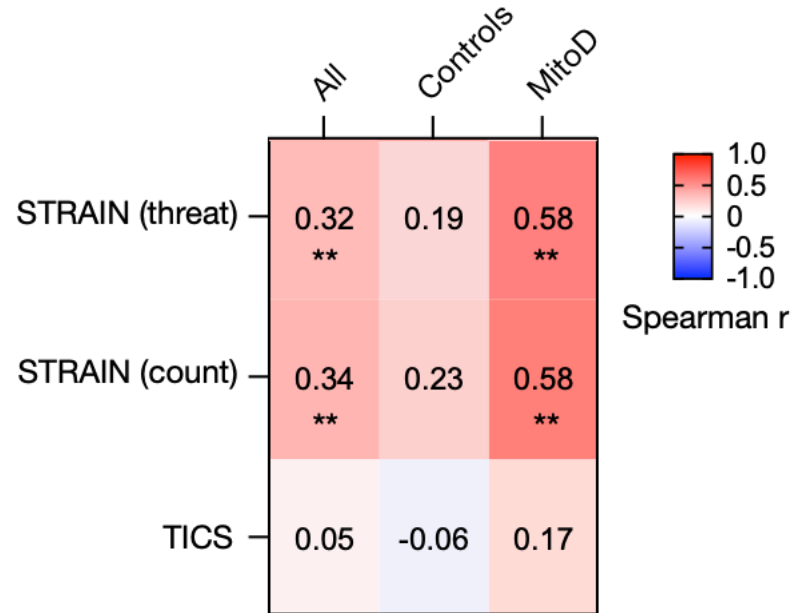
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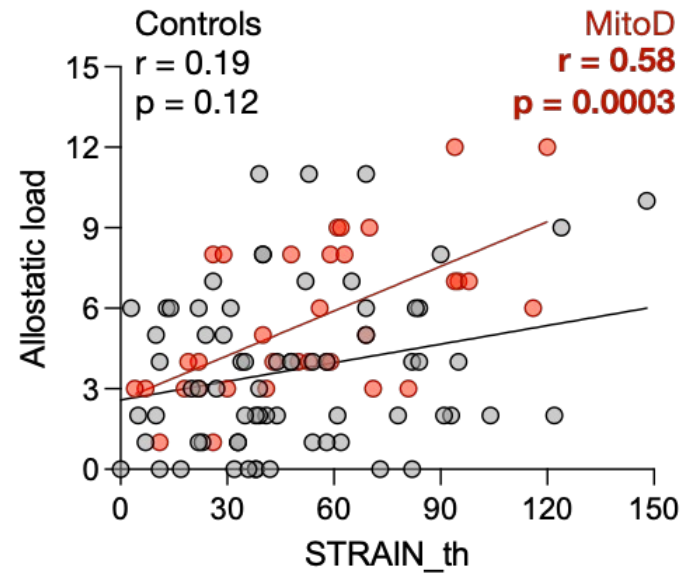
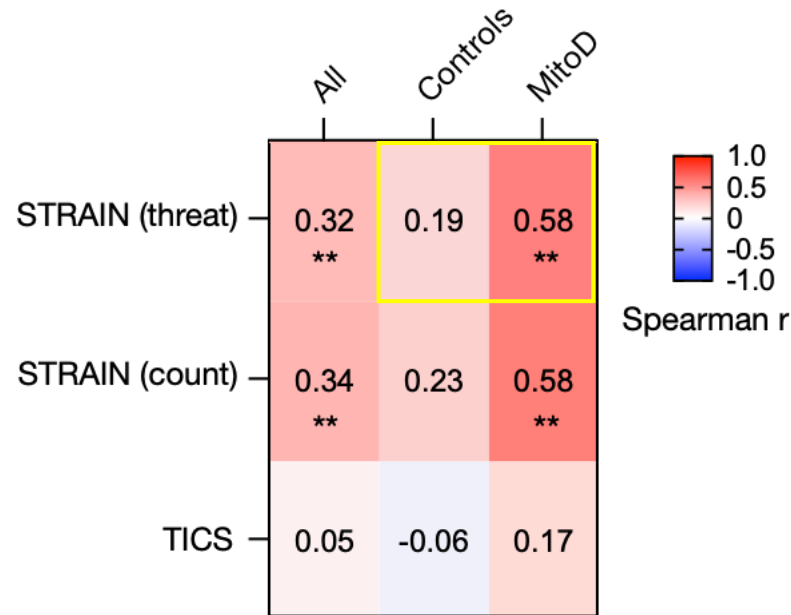
Childhood Trauma Questionnaire (CTQ)

- **Measures childhood trauma and maltreatment**
 - Retrospective (childhood)
- Participants rate the frequency and duration of specific traumas
 - Subscales: physical & emotional abuse, physical and emotional neglect, sexual abuse

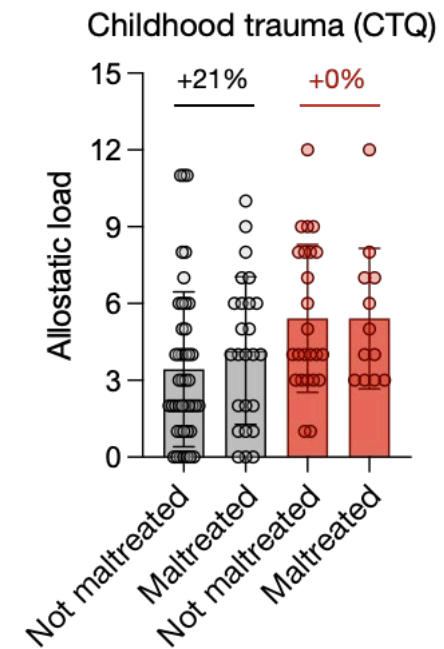
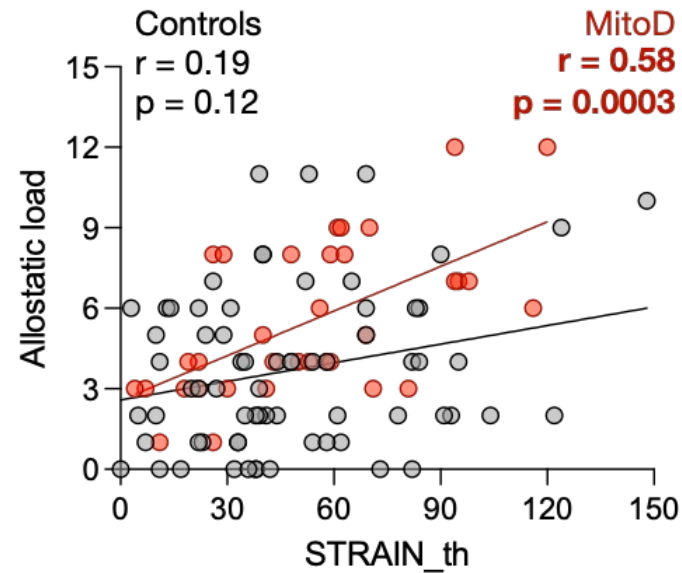
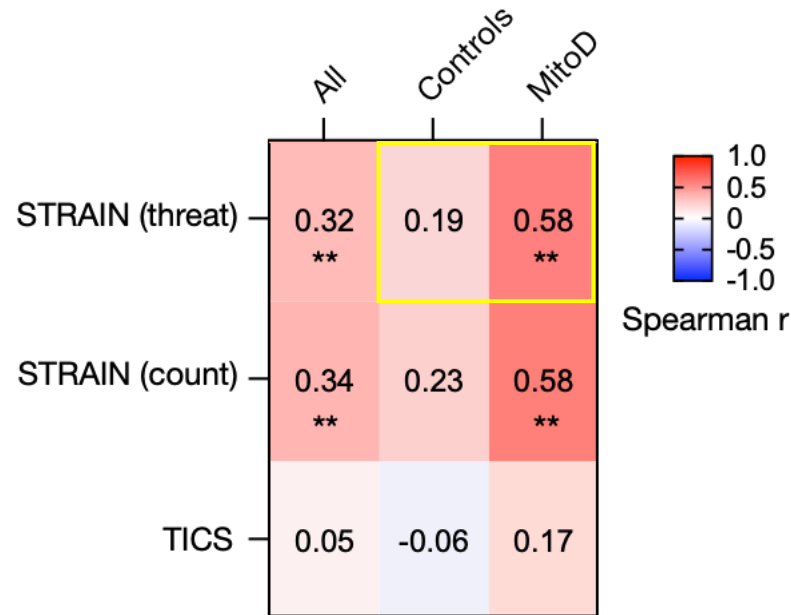
AL is correlated with stress for people with mitochondrial diseases



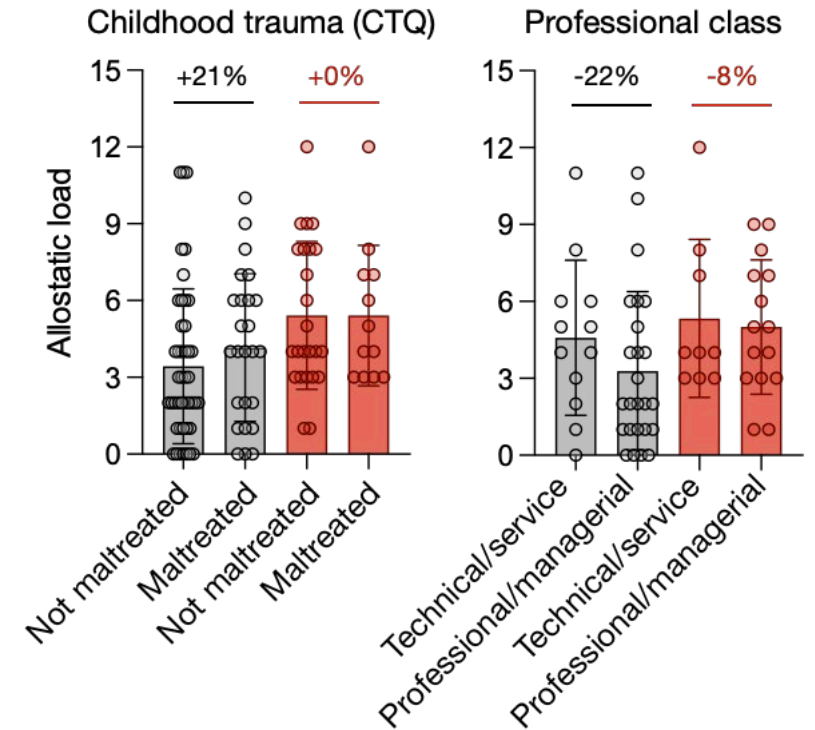
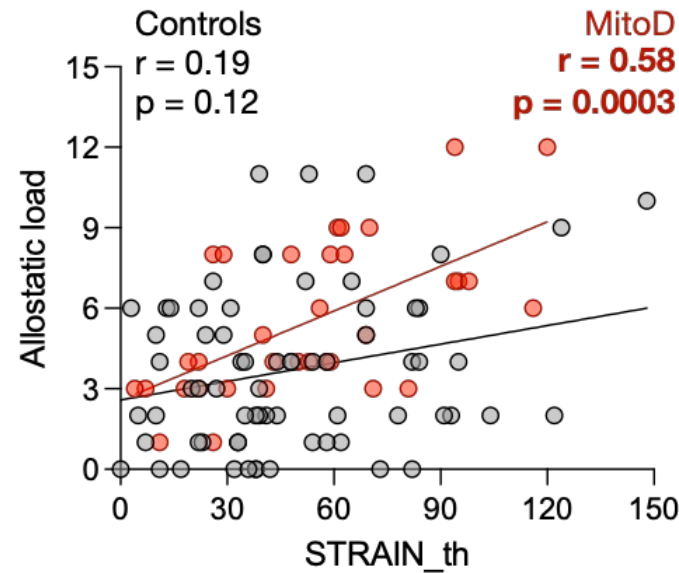
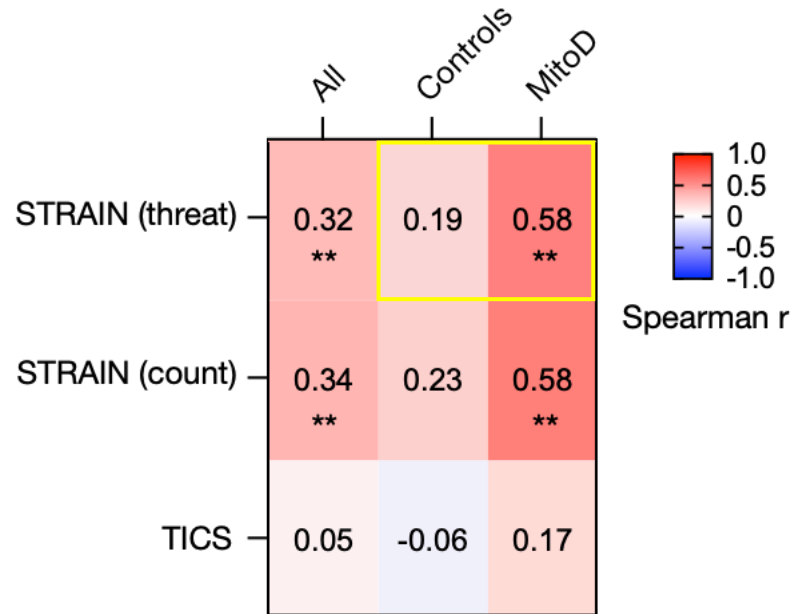
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What did we see?

- Allostatic load (AL) is higher in people with mitochondrial diseases
 - AL correlates with age only for controls, not for people with MitoD
- System-specific dysregulation varies with mitochondrial disease
 - ++metabolic dysregulation
- AL is more strongly correlated with lifetime stressor exposure for people with mitochondrial diseases

What does this mean?

- The link between energetic stress and multi-system dysregulation suggests that
 - 1) Energetic stress could lead to AL, or
 - 2) AL incurs an energetic stress
- Even dysregulation arising from genetic mutations could be affected by what is going on around a person
- Need for interventions to provide support and decrease chronic stressors for people with MitoD

Thank you!



Robert-Paul Juster

Teachers

- Jill Turner
- Sarah Schumacher-Bass
- Kim Hopper
- Daniel Speiser
- Steve Rachmad
- John Darnielle
- Larry Mitchell
- Ned Astra

