PKU & the Brain
Looking beyond white matter

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Disclosure: On occasion, I also serve as an outside consultant for BioMarin Pharmaceutical Inc., and they have funded some of our research on PKU.
Brain Organization 101

- Major Tissue Distinction
  - **Grey Matter** – Brain areas where ‘data processing’ occurs
  - **White Matter** – Insulated ‘wires’ connecting different brain areas with each other.
Brain Organization 101

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Increased risk of white matter injury

30yo TYP

30yo w/ PKU

For review, see Anderson & Leuzzi (2010)
Impact may be moderated by:
- Timing of treatment (earlier = better)
Increased risk of white matter injury

- Impact may be moderated by:
  - Timing of treatment (earlier = better)
  - Adherence to treatment (stricter = better)

Peng, Peck, White & Christ (2013)
Impact may be moderated by:

- Timing of treatment (earlier = better)
- Adherence to treatment (stricter = better)
- Consistency of treatment (stable = better)

Note: White matter tracts highlighted in yellow showed a statistically significant ($p < .05$) relationship between their integrity and mean phe exposure and variability (SD) in phe exposure, respectively.

...but what about grey matter?
Our Recent Research
Cortical Grey Matter Analysis
Cortical Grey Matter Analysis
## Participant Sample

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<th>Prior Year Phe Levels</th>
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Christ et al (MGM; 2016)
GM Volume in Posterior Brain

Lateral View

Medial View

Ventral View

Christ et al (MGM; 2016)
Cerebellar Grey Matter Analysis
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GM Volume in Cerebellum

\[ p < .05 \]
White matter *matters*…

…but not the whole story!
Decreased GM Volume in both Cortex & Cerebellum

Relationship with phe levels = UNCLEAR

Relationship to behavior & cognition = UNCLEAR

*Immediate Goal = More brains!!!*
Future Directions

- Why are some individuals more affected than others?
- Are these problems reversible with treatment?
## Acknowledgments

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- & the rest of our team

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- Dawn Peck

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- University of Kansas Medical Center
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- University of Nebraska
Thank you!

Questions?

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