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 are funding some of our current 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.
Major Tissue Distinction

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**Major Tissue Distinction**

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Increased risk of white matter injury

30-yr-old non-PKU

30-yr-old with PKU

Anderson & Leuzzi (2010)
Increased risk of white matter injury

30-yr-old non-PKU

30-yr-old with PKU
Impact may be moderated by:

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

*Image from Beckhauser et al (2011)*
...but what about grey matter?
Our Current Research
Grey Matter Analysis
Grey Matter Analysis
Grey Matter Analysis
Grey Matter Analysis
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Grey Matter Analysis
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<th></th>
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<tr>
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<td>111</td>
<td>102-120</td>
<td>24.2</td>
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<td>111</td>
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Christ et al. (unpublished)
Results thus far...

PKU Cortical Thickness

Left Hemisphere

Right Hemisphere

Christ et al. (unpublished)
Results thus far...

**Left Hemisphere**

**PKU**
- Cortical Thickness

**Non-PKU**
- Cortical Thickness

**Right Hemisphere**

Christ et al. (unpublished)
Results thus far...

Left Hemisphere

PKU Cortical Thickness

Non-PKU Cortical Thickness

AVG DIFF

Christ et al. (unpublished)
Results thus far...

GM Volume

- **Frontal**: $p = .05$
- **Occipital**: $p = .04$
- **Parietal**: $p = .07$
- **Temporal**: $p = .08$

Christ et al. (unpublished)
Age-Related Changes in Gray Matter Thickness

Gray Matter Volume

Gogtay et al. (2004)
Results thus far...
Preliminary Conclusions

- Decreased GM Volume in ETPKU
- 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?
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Thank you!

Questions?

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EXTRA SLIDES
Gray Matter Findings

- Decreased volume in...
  - Whole brain
    (Perez-Duenas et al., 2006; Pfaender et al., 2005)
  - Hippocampus & pons
    (Pfaender et al.; 2005)
  - Motor, premotor cortex, & thalamus
    (Perez-Duenas et al., 2006; Pfaender et al., 2005)
Increased risk of white matter injury
Increased risk of white matter injury
Most Recent Research on Microstructure of White Matter

Peng, Peck, White & Christ (in press)
Effect on WM moderated by phe level
White matter *matters*!

- Complex behavior relies on a host of underlying processes that are each carried out in a single region of the brain. In other words, complex behavior is the result of a network of brain regions.
Grey Matter Analysis
Results thus far...
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