Alterations in cortical grey matter volume in adults with early-treated phenylketonuria

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WHAT IS KNOWN

Phenylketonuria (PKU)

Rare inherited disease
Deficient liver enzyme
High Phenylalanine (Phe)
Severe intellectual disabilities

Consequences if untreated

Treatment: DIET

Avoid protein
Mostly vegetables and fruits

ISSUE

Despite strict treatment, adults with PKU still show abnormalities in the structure and function of the brain.

- The white matter of the brain seems to be especially vulnerable. 1,2,3
- BUT due to mixed results: impact of the disease on the cortical GREY matter of the brain is still not clear. 4,5,6

HYPOTHESES

Patients vs. controls:
- Cortical volume of patients

In patients only:
- Cortical volume
- Phenylalanine, Tyrosine (Tyr), and Phe:Tyr ratio

METHODS

Neuroimaging

MRI: T1-weighted sequence (MPRAGE)

Preprocessing and analysis: FreeSurfer software 7

Amino acid profile (only patients)

- Phenylalanine
- Tyrosine
- Phe:Tyr ratio

Sample

PKU n = 23 Controls n = 52

| Age (Mean ± SD) | 31.9 ± 9.0 | 30.2 ± 7.8 |
| Gender | 11 female 12 male | 26 female 26 male |
| Phe (Mean ± SD) | 726.7 ± 206.0 | - |
| Tyr (Mean ± SD) | 42.4 ± 10.2 | - |
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RESULTS

Cortical volume for each lobe per hemisphere

- PKU vs. controls: No significant differences in cortical volume of all lobes
- More detailed analysis of 68 brain regions: also no significant differences in cortical volume (after correction for multiple comparison)
- No relationship between metabolic parameters and cortical volume

DISCUSSION

- PKU vs. controls: No differences in cortical volume, neither in total cortical volume, volume for each lobe, nor for all the 68 cortical subdivisions.
- No relationship between cortical grey matter volume and metabolic parameters
  - In adults with PKU: cortical volume seems less affected than reported in the literature
  - Possible reasons: technical differences (MRI acquisition and analysis) and the homogeneity of our sample (only early-treated adults)

REFERENCES