Neural correlates of working memory in early-treated adult patients with Phenylketonuria

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BACKGROUND

• Phenylketonuria (PKU) is an inborn error of metabolism affecting the conversion of phenylalanine (Phe) to tyrosine.¹
• Despite early initiated treatment and a Phe-restricted diet, there is a high variability in terms of cognitive outcome in early-treated adults with PKU.²
• Functional magnetic resonance imaging (fMRI) provides insights into functional brain organization in individuals with early-treated PKU.³
• fMRI of working memory as a possibility to study neural activation in the fronto-parietal working memory network and its associations with task performance and metabolic parameters.

AIM

• Examine working memory performance and related neural activation in early-treated adults with PKU
• Explore the relationship between neural activation and task performance
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METHODS

Study design
- Cross-sectional study
- Inclusion criteria: diagnosis of PKU after positive newborn screening, initiation of Phe-restricted diet within 30 days of life, age > 18 years

Participants
- 20 early treated adults with PKU (mean age: 31.4 ± 9.0 years)
- 40 healthy controls (mean age: 29.8 ± 8.2 years)

Assessments
- Blood sampling: Phe, tyrosine, and tryptophan concentration
- fMRI of working memory: visuospatial n-back task

RESULTS

- fMRI task performance: lower task accuracy \(F(1,56) = 7.541, \ p = .008\) but comparable reaction times \(F(1,56) = .168, \ p = .684\) in the 3-back condition in the PKU group compared to the control group.
- No associations between task performance and neural activation.
- Region-of-Interest analyses: See figures 1 and 2.

Figure 1. Regions of the fronto-parietal working memory network
Regions are derived from the NeuroSynth database. Light green = left insula; light blue = right insula; dark green = right inferior frontal gyrus; yellow = left middle frontal gyrus; purple = left middle frontal gyrus; dark blue = right middle frontal gyrus; red = right superior frontal gyrus; brown = left inferior parietal gyrus; orange = right inferior parietal gyrus.
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**RESULTS**

- Our results demonstrate **subtle alterations** in performance and neural activation, particularly in frontal regions of the working memory network in early-treated adult patients with PKU.
- These findings align with previous studies indicating that patients with PKU display **changes in functional parameters** of the brain despite early-initiated treatment.

**CONCLUSION**

- Our results demonstrate subtle alterations in performance and neural activation, particularly in frontal regions of the working memory network in early-treated adult patients with PKU.
- These findings align with previous studies indicating that patients with PKU display changes in functional parameters of the brain despite early-initiated treatment.

**REFERENCES**