

NEUROCOGNITIVE FUNCTIONING IN SCHOOL-AGED CYSTINOSIS PATIENTS

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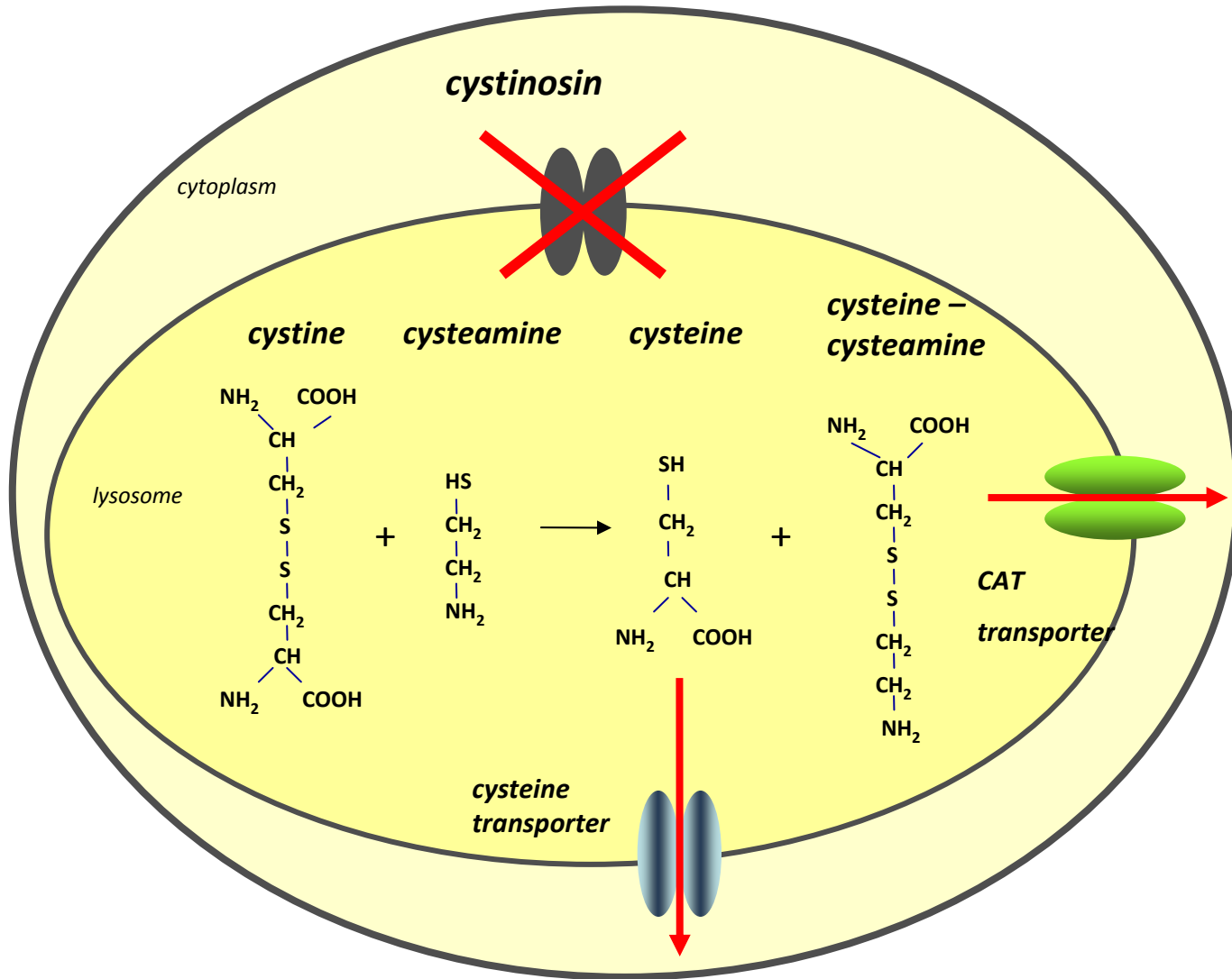
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Cystinosis

- 1:200,000 live births
- Mutation *CTNS* gene encoding cystinosin
- Renal Fanconi syndrome, end stage renal disease
- Multi-organ involvement (including cornea crystals, hypothyroidism, diabetes mellitus, hypogonadism, myopathy, central nervous system)

Cystinosis



Neurocognitive functioning

- Normal intelligence (Verbal > Performance)
- Visual information processing
- Tactile recognition
- Poor school results (spelling, arithmetic)

•Trauner,D.A., Chase,C., Scheller,J., Katz,B., & Schneider,J.A. Neurologic and cognitive deficits in children with cystinosis. *J. Pediatr.* 112, 912-914 (1988).

•Wolff,G., Ehrich,J.H., Offner,G., & Brodehl,J. Psychosocial and intellectual development in 12 patients with infantile nephropathy and cystinosis. *Acta Paediatr. Scand.* 71, 1007-1011 (1982).

•Spilkin *et al.* Visual and verbal learning in a genetic metabolic disorder. *Neuropsychologia* 47 (2009) 1883–1892

•Ulmer *et al.* Intellectual and motor performance, quality of life and psychosocial adjustment in children with cystinosis. *Pediatric Nephrology*, in press

Neurocognitive functioning

- Cystine accumulation in brain tissue?
- Cysteamine passage of blood-brain barrier?

Broyer, M. *et al.* Clinical polymorphism of cystinosis encephalopathy. Results of treatment with cysteamine. *J. Inherit. Metab Dis.* 9, 65-75 (1996).

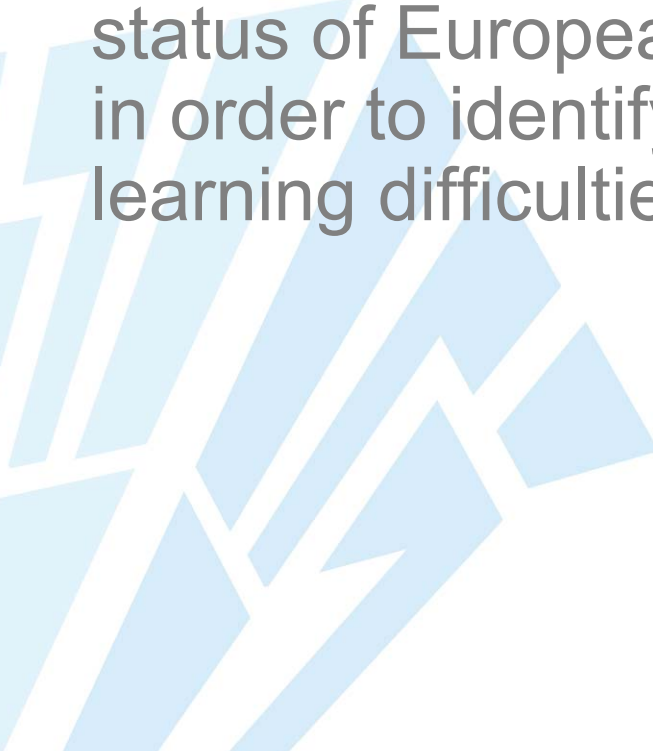
Bava *et al.* Developmental changes in cerebral white matter microstructure in a disorder of lysosomal storage. *Cortex*, in press.

Maurice *et al.* Cystine accumulation in the CNS results in severe age-related memory deficits. *Neurobiology of aging*, in press.


Berger *et al.* Cystinosis of the brain and spinal cord with associated vasculopathy. *Journal of the Neurological Sciences*, in press.

Aim

Analysis of the neurocognitive functioning and renal status of European, school-aged cystinosis patients in order to identify specific deficits which can lead to learning difficulties.



Patients

- 14 school-aged cystinosis patients
 - 13 native kidney
 - 1 pre-emptive kidney transplantation
 - GFR 22-156 ml/min/1.73m²
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- A decorative graphic in the bottom-left corner consisting of several overlapping, semi-transparent blue geometric shapes, including triangles and parallelograms, arranged in a fan-like pattern pointing towards the center.

Methods

- WISC-III

Intelligence (full scale, verbal, performance)

- Developmental test of visual-motor integration (VMI)

Visual-motor integration skills

- Stroop color-word test

Concentration

Interference

- Bourdon-Vos test

Sustained attention

Speed

Accuracy

Methods

- Rey-Osterrieth complex figure

Planning

Visual memory

- Computerized drawing task

Processing speed

Motor planning

Fluency

Motor speed

- Child Behavior Checklist (CBCL)

Behavioral/Emotional functioning

Results

- IQ

Mean full scale IQ 90.2 (range 60-132)

Mean verbal IQ 93.9

Mean performance IQ 88.4

Verbal IQ >> Performance IQ: 5 patients

Performance IQ >> Verbal IQ: 0 patients

Results

- Visual-motor coordination

Poor score 8/14 patients (57%)

- Visual memory

Poor score 8/14 patients (57%)

- Processing speed

Poor score 9/13 patients (69%)

- Planning

Poor score in 8/14 patients (57%)

- Teacher: problems in 2 or more areas

7/14 patients (50%)

Conclusions

- Visual-motor integration and executive (planning) functions are at risk in cystinosis patients.
- Neurocognitive diagnostics aimed at these functions are indicated in all patients from the age of 7-8 years.
- Early recognition and supervision from special education services can diminish learning difficulties and improve school carrier.
- The role of brain involvement in cystinosis and the effect of cysteamine on brain tissue remains unclear.