SUBTLE NEUROPSYCHOLOGICAL ABNORMALITIES IN PATIENTS WITH TYPE I GAUCHER DISEASE

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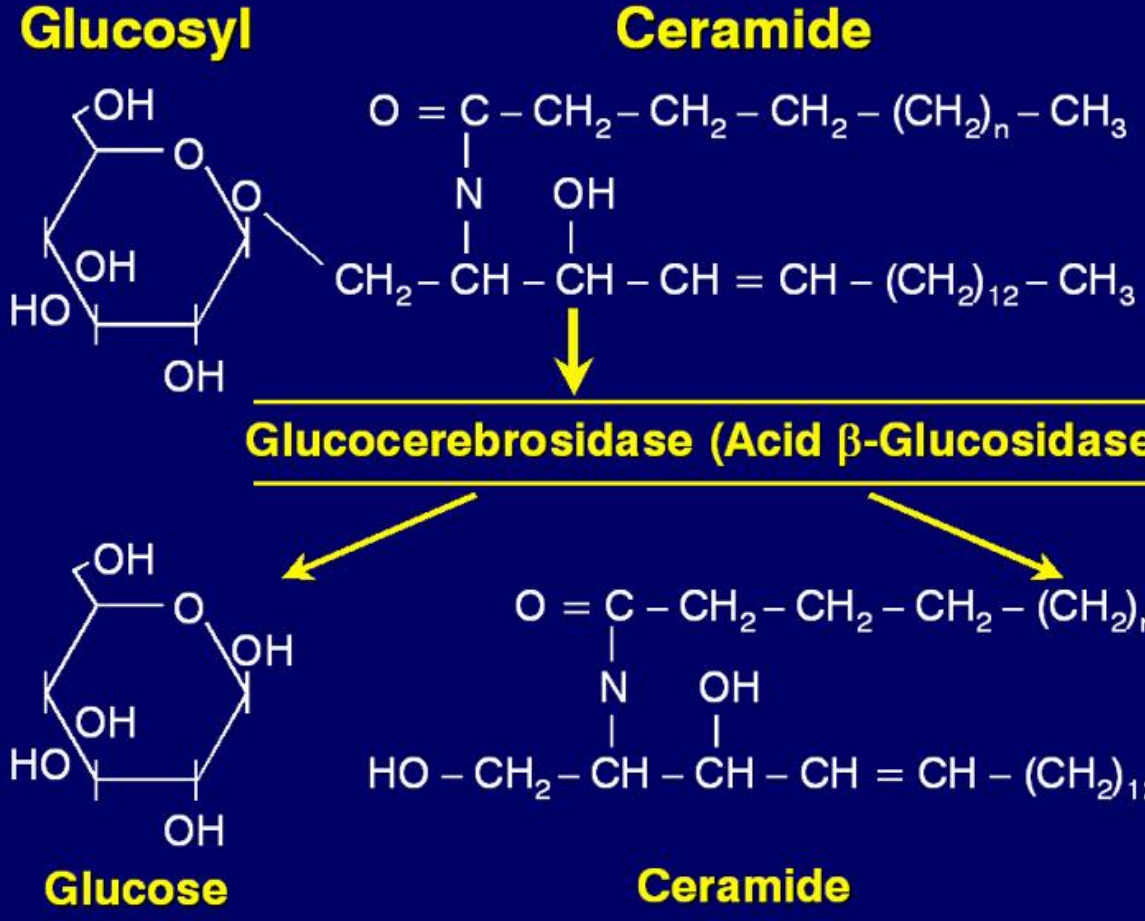
This presentation is dedicated to the memory of the late Dr. Philip Rosenberg

Accumulation of Undegraded Substrate

Glucocerebroside (Glucosylceramide)



Gaucher Disease Subtypes

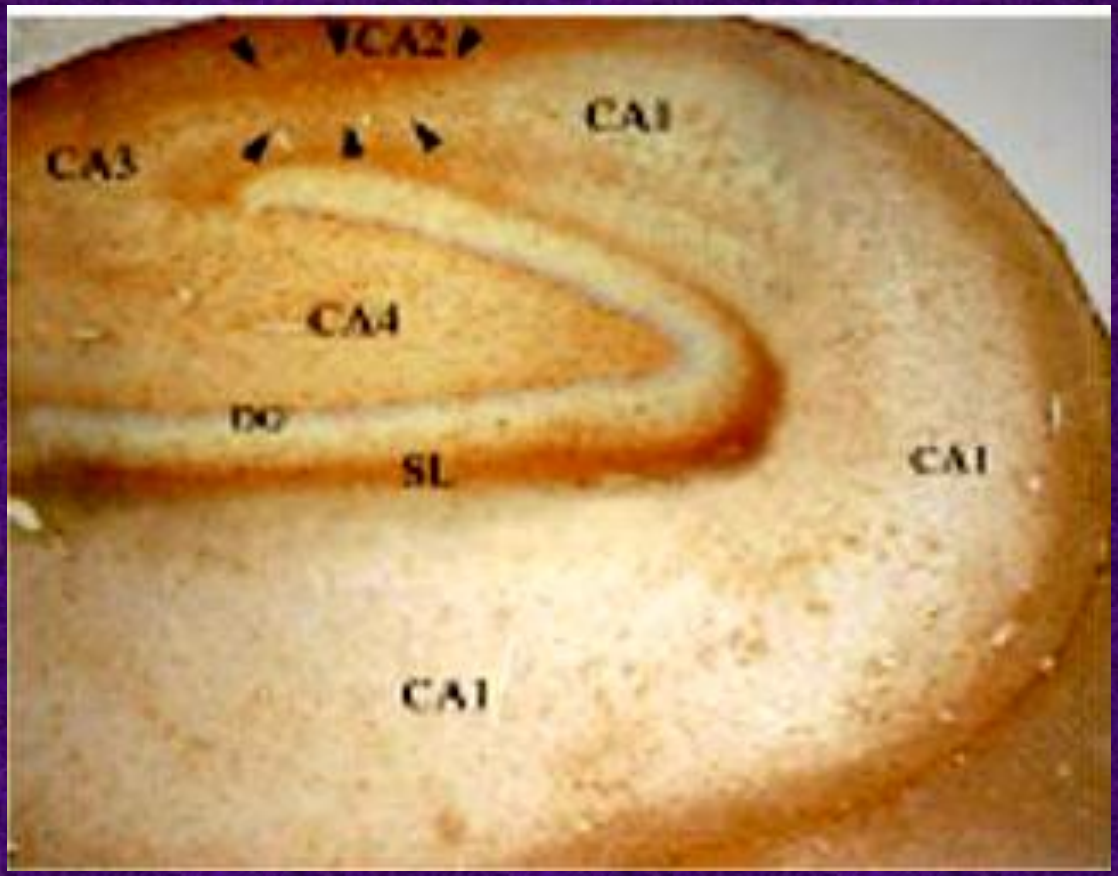
Nonneuronopathic (Type 1)

- Panethnic (approx. 1 in 50,000)
- Prevalent in Ashkenazi Jews (approx. 1 in 500)
- Onset at any age

Neuronopathic (Types 2 and 3)

- Type 2 (acute)
  - Panethnic (approx. 1 in 100,000)
  - Onset in infancy
  - Life expectancy 2 to 3 years
- Type 3 (chronic)
  - Panethnic (approx. 1 in 100,000)
  - Onset in infancy/childhood

New phenotype – visual spatial dysfunction



Gaucher Disease Treatment
Aimed to prevent sphingolipid storage

- Enzyme Replacement Therapy
  Imiglucerase
- Substrate Inhibitor
  OGT-918 (Miglustat)

Subtle neuropsychological abnormalities in patients with type I Gaucher disease

The Ethics Committee recommended that all patients in OGT-918 treatment undergo neuropsychological testing, following the case of Mr. S.

Objective:

This study was aimed to tease out possible drug-related cognitive dysfunction among patients with type I Gaucher disease.

Subtle neuropsychological abnormalities in patients with type I Gaucher disease

Largely non-verbal tasks were tested:

- Memory
- Executive functions
- Working memory
- Visuospatial orientation

Executive Functions – Dencla's ISIS Model:

- Initiative - יזמה
- Shift - מעבר בין מטלות ומצבים
- Inhibition - עכבה (Go-No-Go)
- Sustained attention - קשב מתמשך

to plan, organize and develop strategies or rules and managing time and space

(Denckla, M. 2001)

Executive Functions – Working Memory

the ability to hold information in one's mind while processing and manipulating it.

(Castellanos, F.X., 2002)

Methods:

Neuropsycological tests:

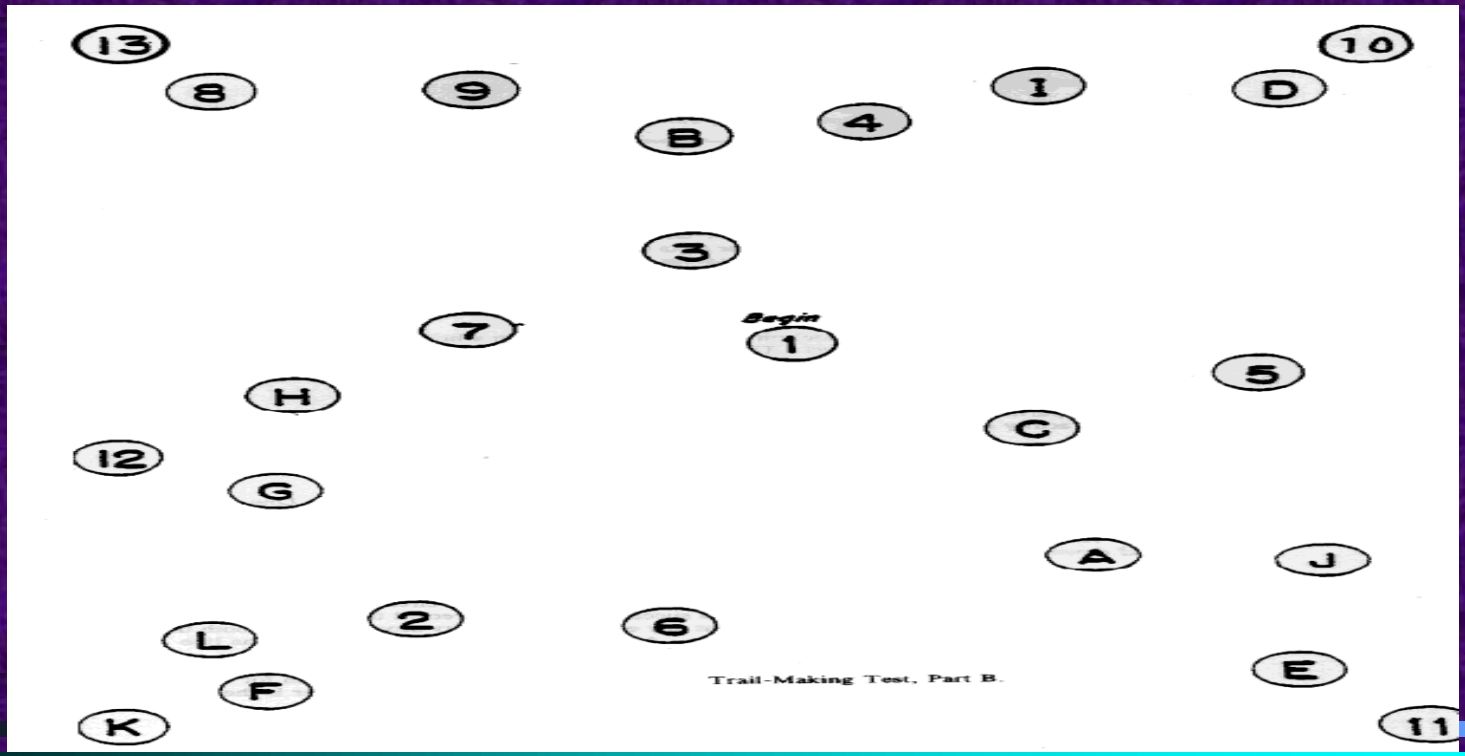
- **Minimental State Examination**
- **Rey Osterreith Complex Figure Test**
- **Rey Auditory Verbal Learning Test**
- **Word Fluency Test (FAS)**
- **Semantic Fluency Test (Animals)**
- **Trail Making Tests A and B**
- **Tower of Hanoi**
- **Wisconsin Card Sorting Test**

Neuropsychological testing
FTL-SHAZBAT

Trail Making Tests A and B:

connect 25 consecutive numbers (A)

then alternate numbers and letters (B)



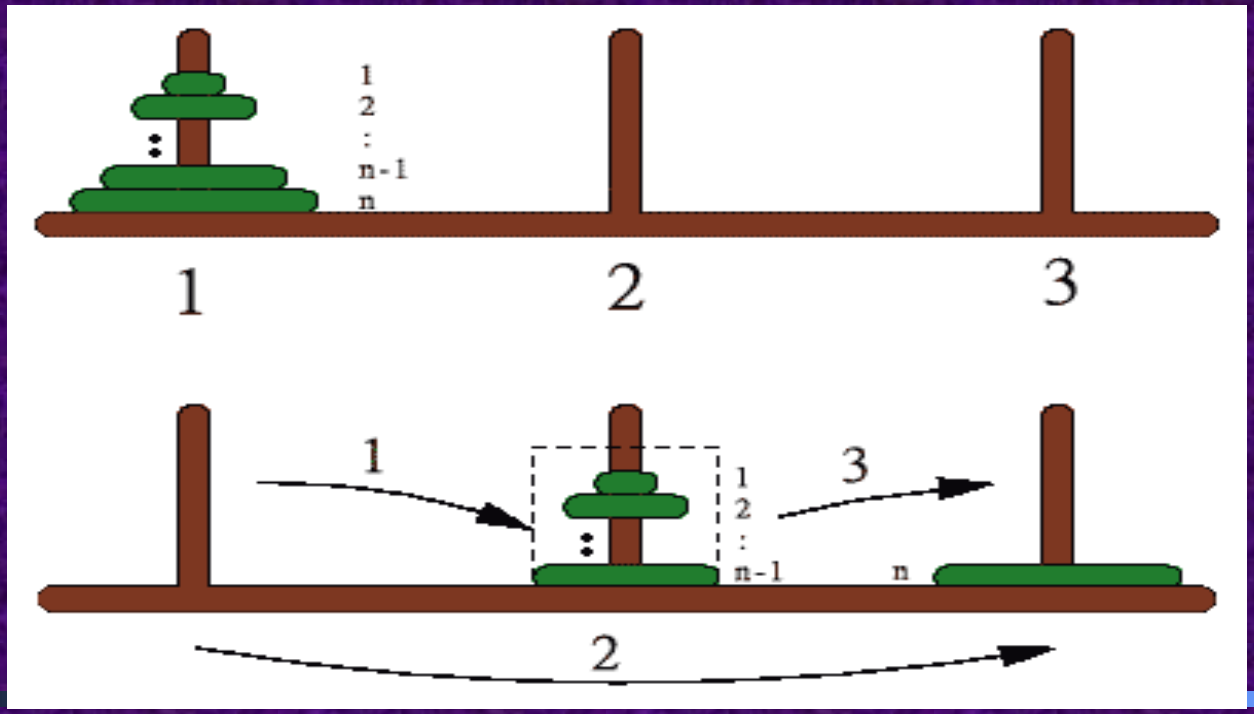
Neuropsychological testing
FTL-SHAZBAT

Semantic Fluency Test: using names of animals to generate a list (1 minute)

Planning and Working Memory (rules)

Tower of Hanoi:

re-positioning rings from 3 poles each with 3 - 5 rings of increasing size

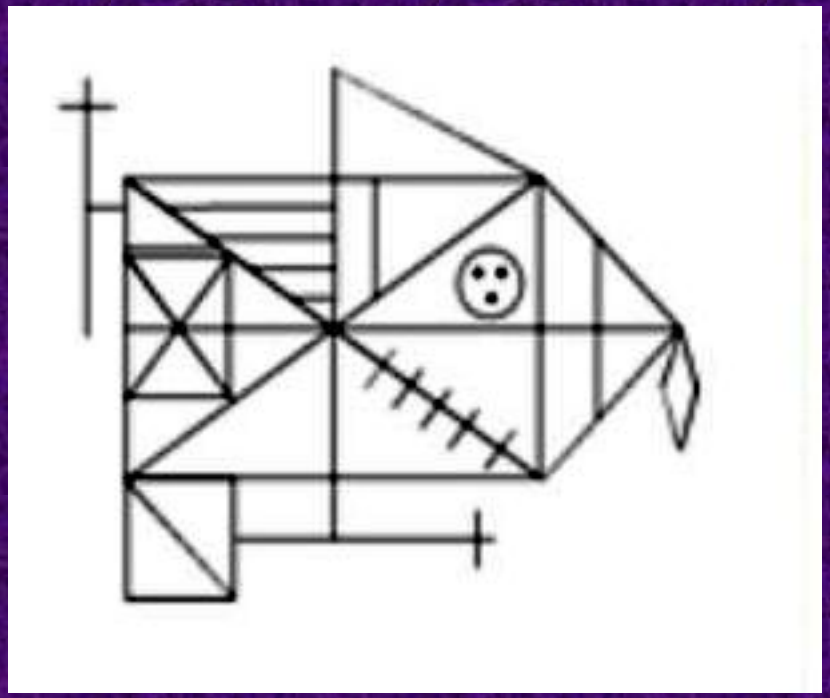


Planning and Working Memory (rules)

Wisconsin Card Sorting Test:

executive function, sorting cards by flexibility and shifting of organizational rules

Rey Osterreith Complex Figure Test



Neuropsychological testing Methods and Results

108 patients :

- **55 patients received OGT-918**
- **31 patients had received ERT**
- **22 patients were untreated**

No significant differences between groups with reference to age or years of education

- **Pearson's correlation for individual scores for OGT-918 relative to treatment period:**

No correlations found

Neuropsychological testing: MMSE*

Cut-off score: 28

GROUP	OGT	ERT	Untreated
number	55	31	22
mean score	28.91	29.29	29.27

*Least sensitive test in the battery

Neuropsychological testing:

Tower of Hanoi

(4 disks; Maximum Number of Steps = 7)

GROUP	OGT	ERT	Untreated
number	47	29	22
mean time	145.8	85.55	81.77
mean steps	9.25	11.17	8.14

Neuropsychological testing:

WCST

z-scores= (-2 ~ +2)

GROUP	OGT	ERT	Untreated
number	55	31	22
category	-1.21	-0.88	-0.66
percent	-0.94	-0.77	-0.79
failure	-0.20	-0.28	-1.40
%con	-2.02	-1.79	-1.91

Neuropsychological testing: Discussion

- Most pervasive finding: low scores in all groups
- There was no statistically significant difference between OGT-918 users and either of the other groups in most tests
- No correlation between scores and duration of OGT-918 treatment

Neuropsychological testing: Discussion

Poor performance in tests.

Specifically: visuospatial and executive functioning

However, these same patients are for the most part accomplished professionals, and some, with international reputation

Can a Gaucher patient be a successful Rabbi or a Teacher?

Yes!

But not recommended:
a Tourist Guide or Architect