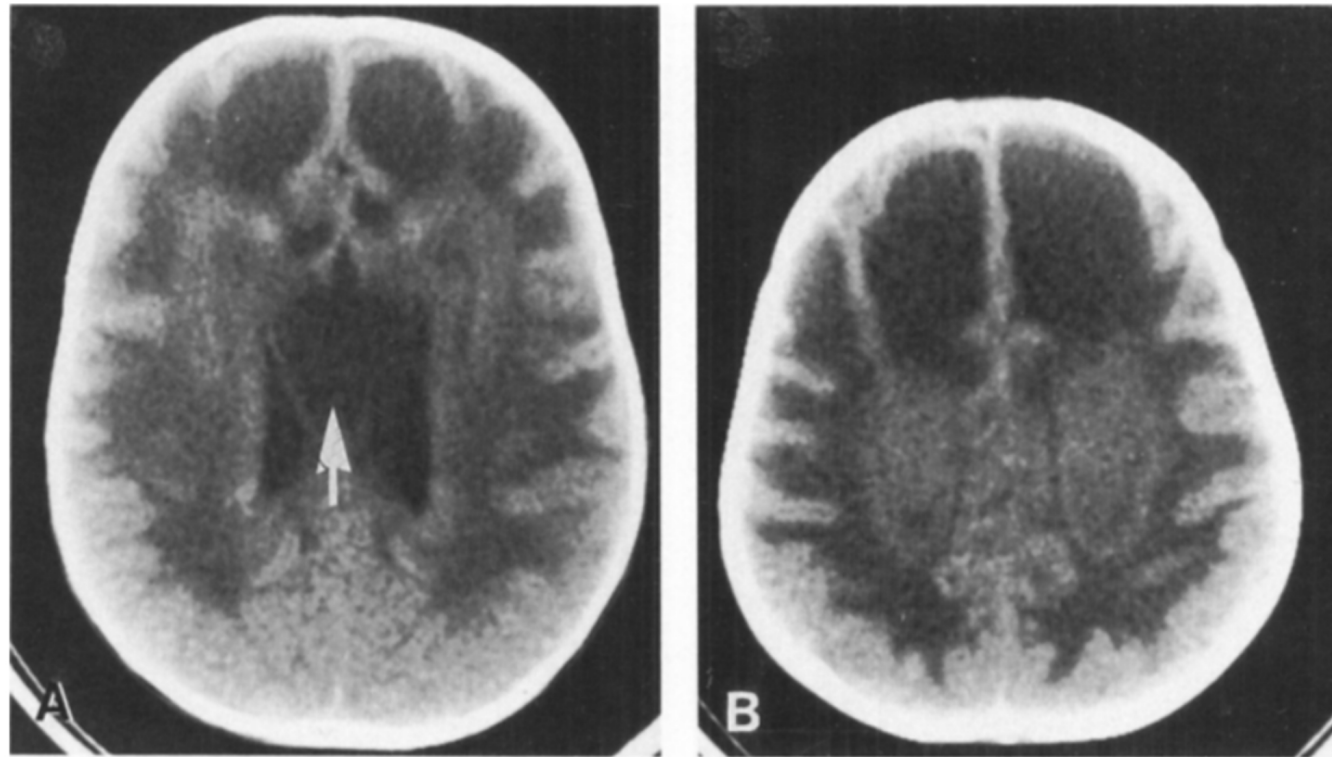

CASE STUDY OF A DISEASE “X”

- J.N. was the first child of healthy parents
- Was normal for 2 months after birth except for a slightly large head circumference
- Her younger brother is normal and no disease history in the family
- At 3 months of age, 2 days after receiving a first diphtheria, pertussis, and tetanus (DPT) immunization, she developed stiffening spells and an abnormal cry
- Seizures few weeks later
- CT scan showed decreased density of the white matter
- Toxoplasmosis, rubella, cytomegalovirus, and herpes simplex tests were negative
- Later clinical seizures subsided, but motor delay remained

- At 8 months old – happy child, but with spastic quadraparesis
- Head too large, veins dilated
- CT showed enlargement of ventricles, low cortical white matter



- MRI – impairment of myelin in frontal and parietal cortex
- Only thin rim of frontal cortex remained

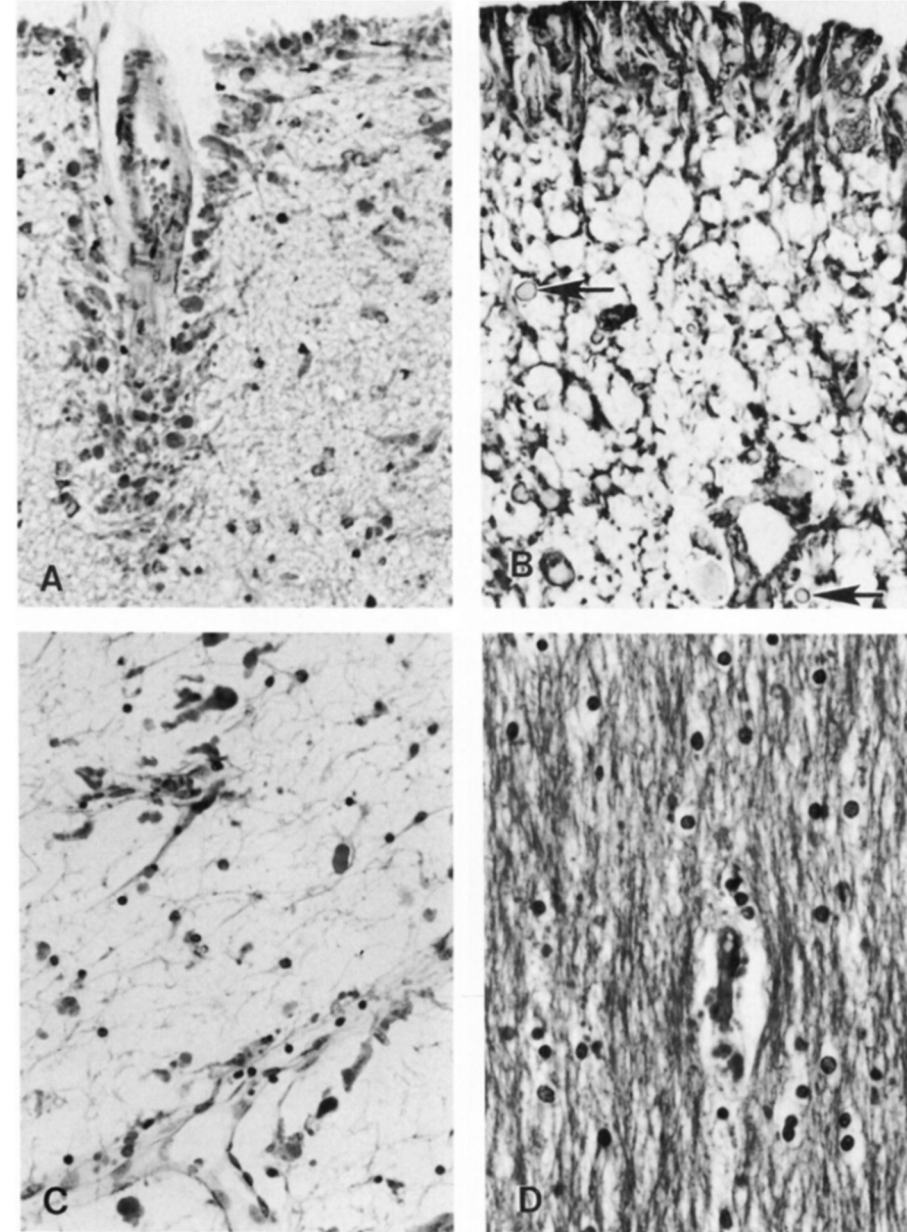


- For several years – she was able move in a walker
- Actively played with social interaction
- Minimal language skills
- During last years all functions were compromised
- Died at 8 years

- Autopsy: huge reduction in cortex width, enlargement of ventricles
- Lysis of myelin and appearance of cavities

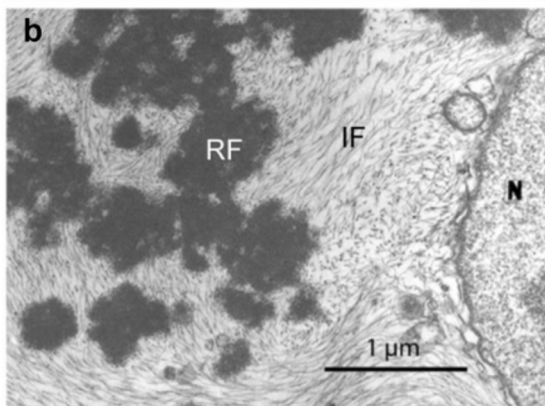
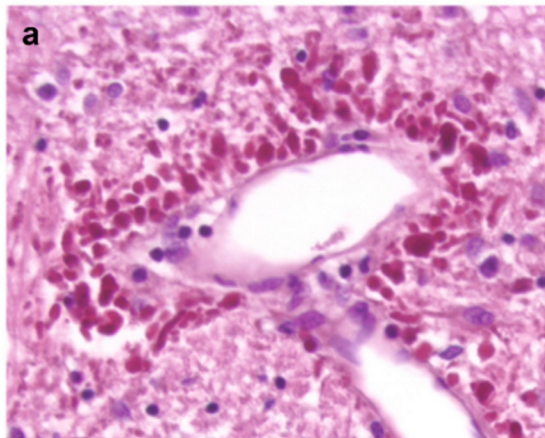


- GFAP staining
- A – fibers around blood vessels in cortex
- B – fibers in spinal cord
- C – Demyelinated white matter in cortex depleted of axons
- D – Preserved white matter in cortex contains fibers

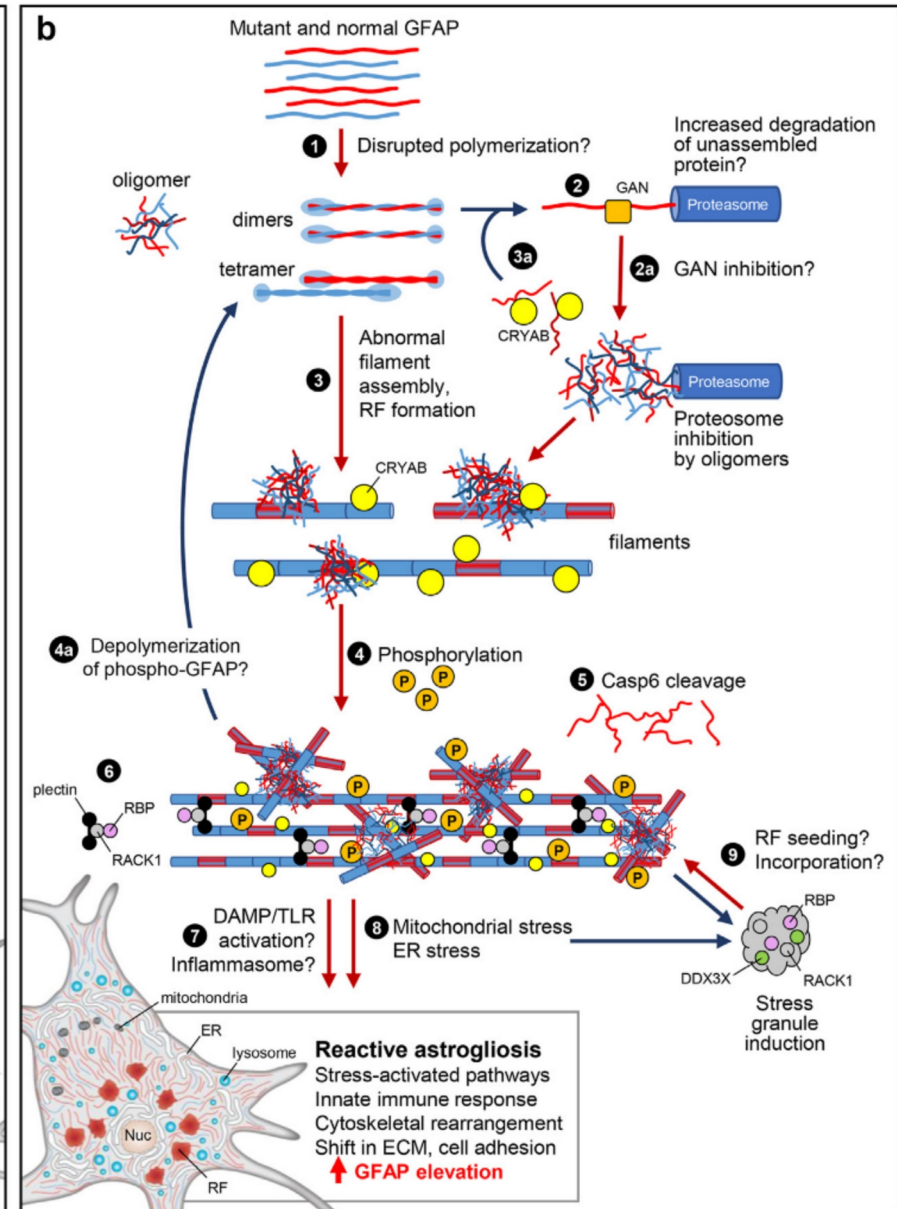
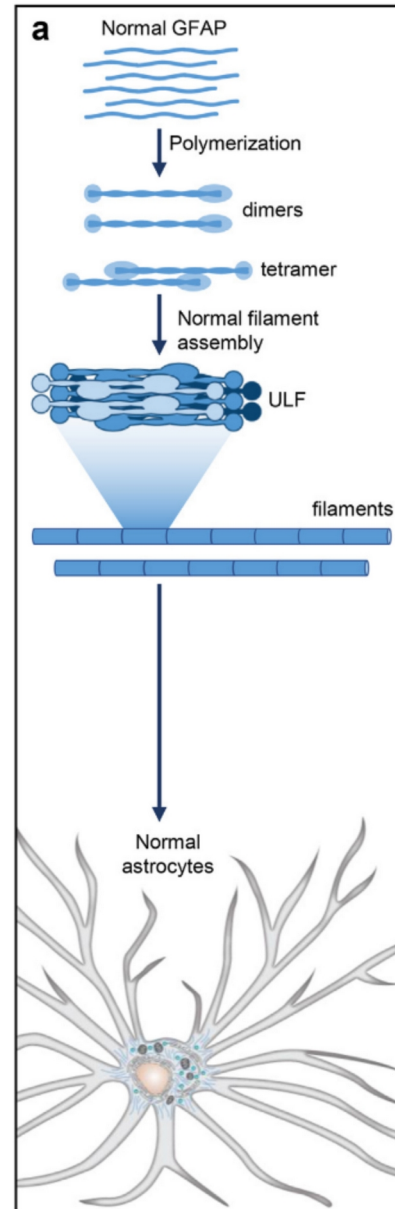


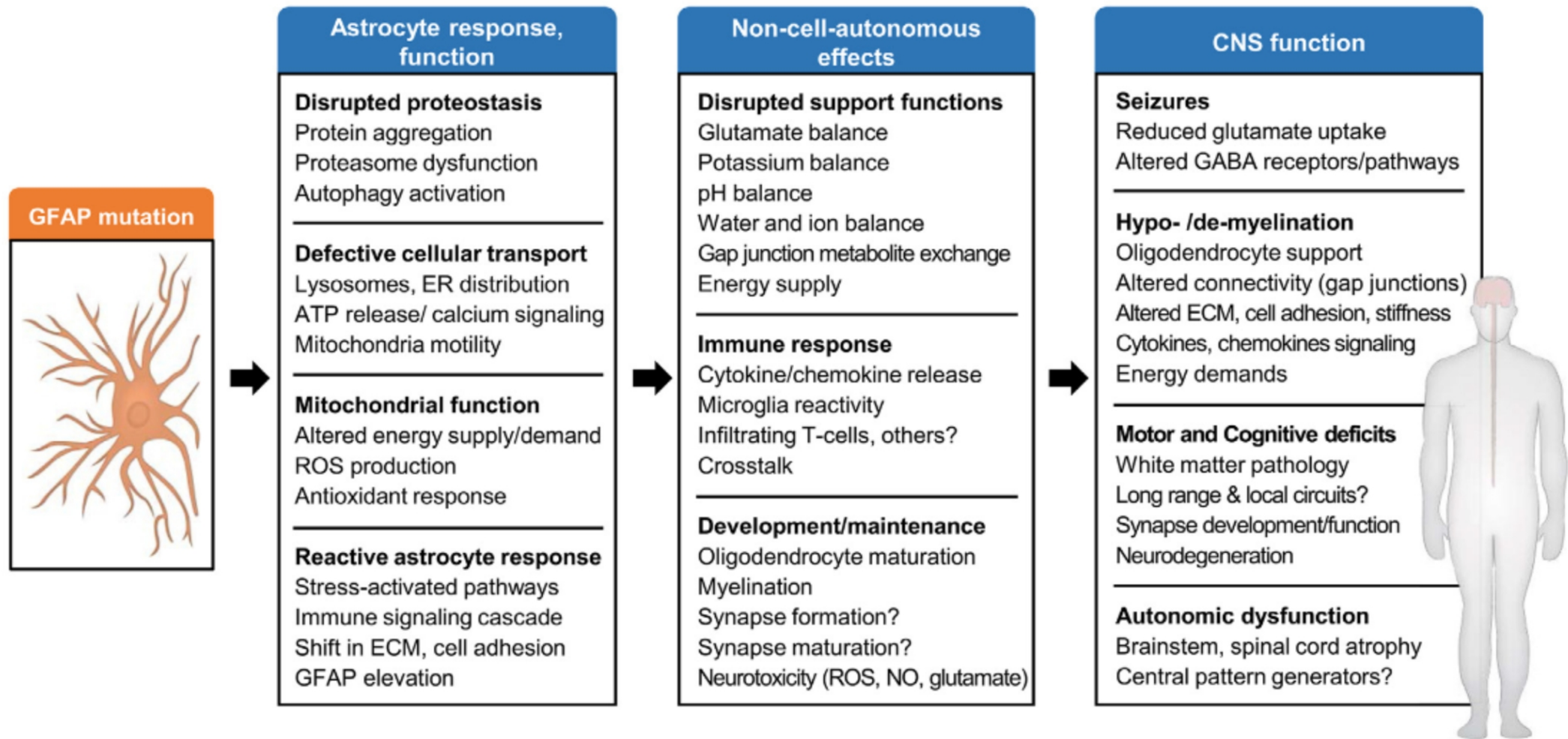
Alexander's Disease (AxD)

Rosenthal fibers – GFAP aggregates, characteristic of AxD:



Current Opinion in Neurobiology





Current Opinion in Neurobiology

No treatment

Short interfering oligonucleotides (siRNA) – to target GFAP mRNA, decrease level of GFAP protein – prospective option