Chronic Traumatic Encephalopathy (CTE) and its connection with ALS

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Chronic Traumatic Encephalopathy

- A rediscovered disease
- Unique neuropathology
- Molecular signature
- Pathogenic mechanism: recurrent trauma

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CASE STUDY

Neuropsychological results and neuropathological findings at autopsy in a case of mild traumatic brain injury

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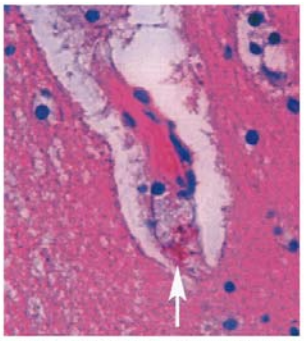

Fig. 3. Histological findings of hemosiderin (arrow) in a perivascular space indicating prior hemorrhagic lesion, most likely trauma induced, according to the neuropathologist's conclusions.

Wild-type and mutant SOD1 share an aberrant conformation and a common pathogenic pathway in ALS

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Many mutations confer one or more toxic function(s) on copper/zinc superoxide dismutase 1 (SOD1) that impair motor neuron viability and cause familial amyotrophic lateral sclerosis (FALS). Using a conformation-specific antibody that detects misfolded SOD1 (C4F6), we found that oxidized wild-type SOD1 and mutant SOD1 share a conformational epitope that is not present in normal wild-type SOD1. In a subset of human sporadic ALS (SALS) cases, motor neurons in the lumbosacral spinal cord were markedly C4F6 immunoreactive, indicating that an aberrant wild-type SOD1 species was present. Recombinant, oxidized wild-type SOD1 and wild-type SOD1 immunopurified from SALS tissues inhibited kinesin-based fast axonal transport in a manner similar to that of FALS-linked mutant SOD1. Our findings suggest that wild-type SOD1 can be pathogenic in SALS and identify an SOD1-dependent pathogenic mechanism common to FALS and SALS.

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Common Pathogenic Mechanisms

- Oxidative Injury
- Inflammation
- Protein Aggregation
- Vasculopathy
- Cell death pathways (Apoptosis)
- ?Transcriptional/translational abnormalities (miRNA)
- ?Epigenetic modifications

Conclusions

- Basic Discoveries continue to revolutionize out understanding of pathophysiology
- Much is yet to be learned by studying postmortem human brain tissue
- This is why it is essential to encourage brain autopsy and donation for research