Tau pathology

Tau Proteinopathy vs Tau Pathology

Both terms are correct but used in different contexts. Below is a comparative summary:

Term	Definition	Typical Use Context
Tau proteinopathy	A neurodegenerative disease characterized by abnormal tau aggregation.	Neuropathological diagnosis, disease classification
Tau pathology	The presence of abnormal tau protein (e.g., hyperphosphorylated, aggregated), regardless of specific disease.	Imaging, biomarkers, histological reports

Tau Proteinopathy

Definition: A class of neurodegenerative diseases characterized by tau protein misfolding, hyperphosphorylation, and aggregation into neurofibrillary tangles (NFTs).

Examples:

- Alzheimer’s disease (mixed proteinopathy)
- Progressive supranuclear palsy (PSP)
- Corticobasal degeneration (CBD)
- Pick’s disease

Use:

- In diagnostic classifications
- In neuropathology reports
- In research defining disease entities

Tau Pathology

Definition: Refers to the histological or biochemical presence of abnormal tau in the brain tissue, cerebrospinal fluid (CSF), or via PET imaging.

Examples:

- Elevated phospho-tau in CSF
- Positive tau-PET imaging
- Detection of neurofibrillary tangles on microscopy

Use:

- Describing findings in research or clinical imaging
- Monitoring disease progression

- Biomarker studies

Summary Table

Aspect	Tau Proteinopathy	Tau Pathology
Scope	Disease entity	Pathological process
Formality	More specific and formal	Descriptive and broad
Field	Neuropathology, taxonomy	Clinical, biomarker, imaging studies
Usage example	“CBD is a 4R tau proteinopathy.”	“Tau pathology was evident in PET scan.”

Tau pathology refers to the accumulation and abnormal aggregation of tau protein in the brain, which is a hallmark of several neurodegenerative disorders, collectively known as **tauopathies**. The most well-known of these diseases is **Alzheimer’s disease (AD)**, but tau pathology is also a key feature of other conditions such as:

- **Progressive Supranuclear Palsy (PSP)** - **Corticobasal Degeneration (CBD)** - **Frontotemporal Dementia with Tau (FTD-Tau)** - **Chronic Traumatic Encephalopathy (CTE)** - **Pick’s Disease**

Tau Protein and Its Function Tau is a **microtubule-associated protein (MAP)** primarily found in neurons. Its normal function includes: - Stabilizing **microtubules** (which help maintain neuronal structure and facilitate transport). - Regulating **axonal transport** by interacting with motor proteins. - Participating in signaling pathways.

Tau is normally **soluble** and highly **phosphorylated** under physiological conditions, but its phosphorylation is tightly regulated.

Pathological Tau Aggregation In tauopathies, tau undergoes **hyperphosphorylation**, causing it to: 1. **Dissociate from microtubules**, leading to destabilization and neuronal dysfunction. 2. **Misfold and aggregate**, forming insoluble filaments and neurofibrillary tangles (NFTs). 3. **Spread** in a prion-like manner across interconnected brain regions.

Mechanisms of Tau Pathology - **Hyperphosphorylation**: Increased phosphorylation reduces tau’s affinity for microtubules, leading to its accumulation in the cytoplasm. - **Truncation and cleavage**: Proteolytic enzymes can break tau into toxic fragments. - **Misfolding and aggregation**: Tau misfolds into β-sheet structures, forming paired helical filaments (PHFs) and NFTs. - **Spreading**: Pathological tau can propagate between neurons, contributing to disease progression.

Tau Pathology in Alzheimer’s Disease - **Neurofibrillary tangles (NFTs)** correlate with cognitive decline. - Tau pathology starts in the **entorhinal cortex** and spreads to the **hippocampus** and **neocortex**. - **Stages of tau pathology (Braak Staging)**:

1. **Stages I-II**: Confined to the transentorhinal region.
2. **Stages III-IV**: Involves the limbic system and hippocampus.
3. **Stages V-VI**: Spreads to the neocortex, leading to widespread neurodegeneration.

Diagnosis of Tau Pathology - **Biomarkers**:

1. CSF tau (total tau, phosphorylated tau).
2. PET imaging using tau tracers (e.g., Flortaucipir, MK-6240).

- **Postmortem histopathology**:

1. Immunohistochemistry for phosphorylated tau.
2. Silver staining techniques.

Therapeutic Approaches 1. **Tau-targeting immunotherapy**: Monoclonal antibodies to clear extracellular tau (e.g., semorinemab, gosuranemab). 2. **Tau phosphorylation inhibitors**: Kinase inhibitors targeting GSK-3β, CDK5. 3. **Microtubule stabilizers**: Epothilone D, Davunetide. 4. **Gene therapy and antisense oligonucleotides (ASOs)**: Targeting tau expression at the RNA level.