

Essential Tremor: Pathology Working Group Session 4 Document

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What do we know?

- Ambiguities remain about the clinical diagnostic criteria for ET which may confound clinico-pathologic studies
- Autopsy clinicopathologic studies have inherent uncertainty about the relationship between early symptomatology and findings at death
- Unlike many other neurologic symptoms, ET is not as clearly recognized as dementia and therefore is not well documented in autopsy series
- Existing autopsy series have demonstrated changes in cerebellar Purkinje cells (number, integrity) which appear to correlate with presence of ET
- Potential confounds in the autopsy series need to be clearly addressed (intercurrent disease, clinical characteristics, etc).

What do we need to know?

- Better understanding of clinical heterogeneity of ET as a clinical disorder
- More extensive autopsy series, with an effort to capturing cases with early stage symptomatic disease dying from other diseases
- How specific across neurologic disease are the reported changes in the cerebellum?
- Anatomic targets to examine based on physiology of tremor – where should neuropathologists be looking?
- What other measures of cerebellar structure beyond Purkinje cell number should be examined and what are the appropriate markers for them? (would include other cell types with specific markers, synaptic structure, axon integrity, etc)
- If ET is a disorder with a clinical spectrum, does the presence of neuropathologic lesions help unite it into one entity (as for the separate diseases now grouped as MSA)? Or will neuropathologic findings define separate entities (as for the FTLDs)?

How can we get there?

- Establishment of robust clinical diagnostic criteria with scoring to be used in centers with interest in movement disorders
- Support for collection of autopsy series (cases and controls); likely to come from centers with interest in movement disorders but will require additional resources
- Taking guidance from physiology studies as to what are the appropriate brain regions to target (both cerebellar anatomic specificity as well as non-cerebellar regions)
- Development of consistent defined sampling methods and staining methods (avoiding Golgi and others which are not useful for statistical analyses)
- Development of a consortium of interested centers for sharing of cases and development of robust measures of assessment (building on the model of CERAD and the ADC program for Alzheimer disease)