NACC Project #2000-08  
Quantification of Neuropathologic Lesions in Alzheimer’s Disease

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Project description  
Recently, there has been increasing recognition that the use of one or two “representative” histologic sections to quantify the extent of CNS lesions may yield erroneous results that are related to systematic biases inherent in the counting procedure. In response to these concerns, methodologies have been developed to achieve non-biased systematic random sampling of structures, approaches (referred to as “stereology”) that are specifically designed to control for such biases. Stereology requires specialized dissection approaches and a considerable investment in facilities and technician time. For this reason, only a few of the Alzheimer's Disease Centers (ADCs) have introduced its use for the evaluation of lesion density. Whether this expensive and time-consuming approach provides data that are sufficiently more accurate and consistent to justify its adoption has yet to be properly evaluated and this study is designed to provide data to answer this question. Using three ADC Neuropathology Core facilities experienced in stereologic procedures, this study addresses these specific aims: 1) Compare the relative precision of data obtained by stereology with that employing the use of a “representative” section, studying neuronal number, the number of neurofibrillary tangle-bearing neurons and of senile (“neuritic”) plaques in the hippocampus and the entorhinal cortex of mildly and severely affected Alzheimer's disease cases; and 2) Determine the inter-laboratory and intra-laboratory consistency of counts using stereological counting techniques of sections counted and recounted in a blinded fashion. Most ADCs have tended to ignore the warnings of Gundersen and West, and continue to rely on the simpler and cheaper approach of examining a single section that is considered “representative” of the structure being examined. It is anticipated that data emerging from this study will greatly assist each of the ADCs in deciding whether or not to adopt non-biased sampling techniques for the quantification of AD-related lesions. Furthermore, it will be determined whether the use of a single “representative” section yields data that truly reflects the extent of pathologic involvement in the hippocampus and entorhinal cortex as a whole. Finally, this study will provide data to assist in determining if data using stereologic approaches can be pooled from multiple laboratories as a strategy for carrying out studies involving the evaluation of relatively large numbers of subjects.

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