

## **HIPPOCAMPAL SCLEROSIS, ARGYROPHILIC GRAIN DISEASE, TDP-43 AND DEMENTIA**

**Lea T. Grinberg**

*USA/Brazil*

Emerging technologies have been creating tools that enable pathologists to uncover brain changes practically invisible to old silver staining methods. These new tools coupled with the growing of well-structured brain banks focused in neurodegenerative diseases are resulting in the identification of new markers of dementia and better understanding on how each of these changes impact cognition. In 2006, the 43-kDa transactive response (TAR)-DNA-binding protein (TDP-43) was identified as the primary constituent of the ubiquitin-positive and tau-negative neuronal and glial inclusions found in brains of patients with frontotemporal lobar degeneration. Follow up clinicopathological studies demonstrated that TDP-43 pathological inclusions are also found in a fraction of cognitively normal elderly and patients with dementia of the Alzheimer's type. In such cases, the distribution of TDP-43 changes differs from the frontotemporal lobar degeneration cases. Nevertheless, TDP-43 impacts cognition independently of other factor. Although the mechanism is yet to be elucidate, TDP-43 inclusions in the hippocampus are associated to loss of cell in the CA1 sector of the hippocampus, called hippocampal sclerosis. On the other hand, argyrophilic brain disease is an age-associated, frequent tauopathy. AGD is mostly underappreciated because it lacks an antemortem clinical markers. Several studies suggest that AGD is a protecting factor against cognitive decline in cases of Alzheimer's disease. Here, all these important neuropathological changes will be discussed in the context of clinical outcome