Review of: "Somatostatin and the pathophysiology of Alzheimer's disease"

E. J. Mufson[1]

1 Barrow Neurological Institute

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The review of the role that alteration in the neuropeptide somatostatin plays in the pathophysiology of AD is well writing and presents a less traveled theoretical concept underlying the basis for the neuropsychological deficits seen in this disease. In general, the review establishes yet another possible neurobiological mechanism that is disrupted in AD. That is that the somatostatinergic system likely is involved in the development of memory impairment in AD. Here, most of the evidence presented is derived from animal studies including tau generated transgenic mice. However, since these and other animal models do not truly replicate the disease these finding should be viewed conservatively. To enhance the overall thesis of this review, a more detail discussing of the role of defects in somatostatinergic system derived from clinical pathological studies would be a valuable contributing to the article. Do alterations in MCI occur prior to mild AD? The authors should also discuss the laminar location of somatostatin positive neurons in the human brain in addition to the data shown in Figure 2. In fact a clearer explanation of the what the white circle indicate in this figure would be helpful for the reader. What was interesting about this figure was the reversal between SOM and Parv positive cells between limbic and neocortex since limbic and paralimbic cortical regions are more prone to tau pathology that isocortical areas. Also amyloid is seen initially in frontal regions compared to temporal areas. The authors discuss possible cholinergic involvement with SOM systems in AD but do not mention their interaction within the cholinergic basal forebrain. In fact, there is a major somatostatinergic pathway that originates with the central nucleus of the amygdala and course through the basal forebrain enroute to the bed nucleus of the stria terminalis. Despite this SOM pathway and Som neurons within the cholinergic basal forebrain, this region displays virtually no amyloid positive plaques. How does this fit in with the author's hypothesis? There is ample evidence that synapse loss significant correlates with cognitive decline better that amyloid deposition. This suggests that reversal between SOM and Parv between limbic cortex and neocortex? Also amyloid is seen initially in frontal regions compared to temporal area. It is interesting that synaptic loss is a better correlate of cognitive impairment that amyloid in AD. This suggests synaptic loss per together with widespread interference and indiscriminate neural activity due to impaired context-dependent inhibitory modulation of cortical and hippocampal plays a combined role in AD pathophysiology. The author may want to emphasize that alterations in the somatostatinergic profile is part of a multi-system dysfunction that occur over the various phases of the onset of AD.