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Tittle: The basal forebrain cholinergic system is affected in age-related Canine Cognitive Dysfunction Syndrome.

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Abstract:

Accruing evidence shows that aged-related canine cognitive dysfunction syndrome (CDS) is accompanied by beta amyloid peptide (Aß) deposits in the cerebral cortex, and degeneration of the serotonergic and noradrenergic neuronal systems. Recently, it has been reported that dogs with mild cognitive impairment present significantly higher plasma Aß levels than both healthy controls and severely impaired dogs. These features increase the similarity between CDS and Alzheimer's disease (AD) which has attracted increasing interest to this canine syndrome. However, detailed studies of the cholinergic system (the most affected neurotransmitter systems in AD) and its response to aging are lacking in the dog. In the present work, we used unbiased stereology to estimate the total number of basal forebrain cholinergic neurons expressing the nerve growth factor low affinity receptor (p75NTR), a well-characterized marker for this neuronal population. Animals included in this study were divided into three groups: young, aged not cognitively impaired (aged-NCI) and aged cognitively impaired (aged-CI) dogs. The average total number of p75NTR positive neurons in one hemisphere for the whole population was 46,717 ± 9,855. No significant differences in neuron number were found between the young and aged-NCI groups. In contrast, aged-CI dogs showed a significant reduction in p75NTR labeled neurons compared to both the young (~26% decrement; P = 0.013) and the aged-NCI (~20% decrement; P = 0.009) animals. Diffuse amyloid deposits were found in all aged dogs independent of cognitive status. These results suggest that the basal forebrain cholinergic system is affected in aged cognitively impaired dogs and provide additional support for the use of age related canine cognitive dysfunction syndrome as a natural model for AD research.