Age-related changes in clinically relevant biomarkers of Alzheimer's disease in the dog.

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Canine ageing is associated with cognitive decline linked to several neuropathological changes that parallel those seen in Alzheimer's disease. The aged canine brain demonstrates deposition of amyloid-β, cerebral amyloid angiopathy, dystrophic neurites, reduced neurogenesis, neuronal loss, activated microglia and astrogliosis. Domain specific cognitive decline is also observed, with short-term working memory and executive function impacted early in canine aging. One contributing factor of Alzheimer's disease is neuroinflammation, including activation of microglia and astrocytes, which are also seen in the aged canine brain. Microglia bind to soluble amyloid-β oligomers and fibrils by various receptors including toll-like receptors (TLR2, TLR4, TLR6 and TLR8), which is postulated to be part of the neuroinflammatory processes in Alzheimer's disease. Toll like receptor activation leads to downstream production and release of pro-inflammatory cytokines through the NFκB signalling pathway. Activated astrocytes accumulate around senile plaques and release cytokines, and other cytotoxic molecules, when exposed to amyloid-β further contributing to the neuroinflammatory response. The current study sought to investigate whether concentrations of the following cytokines varied by age in canine biofluids; IL-6, TNFa, IL-8, IL-10 and IL-12.

Concentrations of the aforementioned cytokines in cerebrospinal fluid and plasma from three age groups of dogs were evaluated in the current study. The young aged group included samples from dogs under 6 years of age. The middle age group included samples from dogs between 6 and 10 years of age. The aged or senior group included samples from dogs greater than 10 years of age.

The results of the study will be presented, and we hypothesise that age-related changes in cytokine concentrations may be used as a potential clinically relevant biomarker for evaluating the effects of putative Alzheimer's disease therapeutics targeting neuroinflammation, particularly when used in conjunction with neuropsychological cognitive assays.

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