Enhancing Brain Functions in Senior Dogs: A New Nutritional Approach

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Aging induces many morphological and metabolic changes in the brain, which may eventually lead to cognitive impairment and dementia called cognitive dysfunction syndrome in senior dogs. Cognitive impairment and dementia can adversely affect the quality of life in both dogs and their owners. Progress has been made over the past years to understand how aging affects brain and its functions in humans and animals including dogs. Existing data indicate that aging-induced changes in the brain are gradual and irreversible. Therefore, it is too late to effectively manage dogs with cognitive impairment and cognitive dysfunction syndrome. The best option to manage brain aging successfully is to reduce or prevent aging-induced changes in the brain by correcting early metabolic changes and eliminating risk factors associated with brain aging and dementia. This article reviews behavioral, morphological, and metabolic changes in the brain induced by aging and discusses a novel nutritional solution for the aging-induced metabolic changes in the brain.

Keywords: brain, aging, neurogenesis, cortical, atrophy, medium-chain triglycerides, ketone bodies, cognitive function, memory, attention, learning

Aging adversely affects all tissues and organs in humans and animals including dogs and cats. Some senior dogs and cats eventually develop cognitive impairment and dementia (cognitive dysfunction syndrome [CDS]), which has adverse effects on the quality of life of both pets and their owners. Cognitive impairment and dementia in pets are the consequences of aging-induced changes in the brain, and most of the changes are irreversible. This article discusses behavioral, morphological, and metabolic changes in the brain induced by aging. In addition, this article reviews a novel nutritional solution for enhancing brain function in senior dogs.

Aging-related Behavioral Changes in Dogs

Behavioral changes in senior dogs usually occur gradually. Senior dogs may sleep more or have altered day and night sleep cycles, withdraw from interaction with family members, and have lower physical activity. These changes are the consequences of aging in dogs.

Cognitive Dysfunction Syndrome in Senior Dogs

Just like in humans, some senior dogs remain to be cognitively healthy, but some of the senior dogs eventually develop cognitive impairment or CDS. Clinical symptoms in dogs with CDS include disorientation, reduced social interaction, increased anxiety, disrupted sleep/wake cycle, and loss of house training.[1,2] Neilson and coworkers[3] reported that about 27.5% of senior dogs from 11 to 12 years of age suffered from mild to severe cognitive impairment and the incident was 67% for dogs between 15 and 16 years of age. CDS can adversely affect the quality of life in both dogs and their owners. Cognitive impairment and CDS are the consequences of aging-related morphological and metabolic changes in the brain.

Aging-related Morphological Changes in Dogs

Cortical Atrophy and Ventricular Enlargement

Aging brains of dogs are characterized by significant cortical atrophy and ventricular enlargement.[4,5] It appears that various brain regions had different rates of atrophy, and both prefrontal cortex and hippocampus suffered more severe atrophy than other brain regions.

Brain aging in dogs is quite similar to that of humans, and cognitive impairment and CDS in dogs resemble mild cognitive impairment and some of the characteristics of Alzheimer's disease (AD) in humans.[6] For instance, the beta-amyloid precursor protein (APP) in dogs is almost identical to the APP in humans, and the beta-amyloid peptide deposits in dogs' brains are diffuse and similar to the early stage of beta-amyloid peptide deposits in humans, but canine aging brains appear to lack the neurofibrillary tangle formation, which is another hallmark of AD in humans.[7]

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Irreversible Reduction in Neurogenesis in Senior Dogs

Adult animal brains continuously produce new cells including neurons from progenitor cells in specific regions; however, senior dogs had significantly reduced neurogenesis compared with young adult dogs.[8,9] Aging-related reduction in neurogenesis is due to a decrease in both progenitor cell proliferation and survival of new neurons.[8] The number of neurons and newly formed neurons in the hippocampus significantly correlated with cognitive functions including learning and memory in dogs. These data suggest that neurogenesis may be involved in the process of learning and memory formation.[8] Diet supplemented with antioxidants or behavioral enrichment failed to enhance neurogenesis in senior dogs, indicating that aging-induced reduction in neurogenesis is irreversible.[8]

Irreversible Loss of Neurons in Senior Dogs

In addition to reduction in neurogenesis, significant neuron loss was observed in brains of senior dogs and may contribute to the cortical atrophy in senior dogs.[10,11] Neuron loss may be due to apoptosis caused by toxic APP, cerebral vascular lesion, and increased oxidative stress and inflammation.[12-16] Cortical atrophy also results in aging-related changes in brain functions, and there is a strong correlation between cortical atrophy and decline in cognitive functions in senior dogs.[17]

In summary, cognitive impairment and dementia are the consequences of severe loss of brain cells and reduced neurogenesis, which gradually occur over a long period and are not reversible. It is too late to effectively manage dogs with cognitive impairment and CDS because of irreversible loss of brain cells and irreversible reduction in neurogenesis in senior dogs. Therefore, it is critical to start nutritional interventions earlier to reduce neuron loss and manage brain aging successfully by correcting early metabolic changes and minimizing risk factors associated with brain aging and dementia.

Aging-related Metabolic Changes and Consequences

Reduction in Cerebral Glucose Metabolism in Senior Dogs

Brains are highly metabolically active and account for only about 2% to 3% of body weight, but account for 25% of daily whole body glucose consumption.[18] Neuronal activity and cerebral glucose metabolism are tightly coupled, and supporting increased neuronal activity depends on increased ATP production from increased glucose metabolism.[19] Therefore, adequate energy supply is essential for normal brain functions.

Normally, glucose is the main energy source of the brain. Unfortunately, cerebral glucose metabolism is reduced in healthy older people[20] and healthy older animals including rodents,[21] dogs,[22] and monkeys.[23] In addition, studies in both rats and dogs indicated that cerebral glucose metabolism was significantly reduced, even in middle-aged animals, compared with young adult animals. For instance, Rapoport and coworkers[21] showed that glucose metabolism in the brain was reduced by up to 30% between 3 and 12 months of age in rats. A study in dogs indicated that glucose metabolism in the brain was significantly reduced at 6 years compared with 1 year in beagle dogs.[22] Milgram[24] reported that cognitive function decreased significantly in middle-aged beagle dogs compared with young dogs. Therefore, cerebral glucose metabolism correlates strongly with cognitive function, and reduced glucose metabolism occurs several years before the appearance of cognitive impairment and dementia symptoms and may partly contribute to the decline of brain functions associated with aging.[25]

Severe Reduction in Cerebral Glucose Metabolism in Dementia

Existing studies indicate that cerebral glucose metabolism is further reduced in subjects with dementia compared with healthy older subjects. Alexander and coworkers[26] reported that cerebral glucose metabolism was significantly lower in older patients with AD than in age-matched healthy older subjects. A longitudinal study indicated that patients with mild cognitive impairment developed clinical symptoms of AD only when a further reduction of cerebral glucose metabolism was observed in patients.[27] In the brain, insulin, insulin-like growth factor-1 (IGF-1), and their receptors play an important role in regulating metabolism, promoting neuronal growth, maintaining learning and memory functions, and protecting neurons against cell death.[28,29] However, insulin and insulin receptors decreased with aging in the brain, suggesting that dysfunction in insulin-IGF-1 signaling pathway may be, at least partially, responsible for the reduced glucose metabolism associated with aging and dementia.[30] This hypothesis was further supported by the link between type 2 diabetes mellitus and increased risk of AD.[31-33]

In summary, cerebral glucose metabolism is positively correlated with brain functions, the age-associated reduction in cerebral glucose metabolism may occur in all animals, at least partially, because of dysfunction in insulin-IGF-1 signaling pathway, the reduction in glucose metabolism happens as early as middle age, and reduced (impaired) glucose metabolism may partially contribute to the development, progression, and symptoms of cognitive decline, cognitive impairment, and dementia.

Ketone Bodies as an Alternative Energy Source for the Brain

ATP production required to support normal brain functions can be derived from either glucose metabolism or ketone body metabolism. Reduction in cerebral glucose metabolism is due to dysfunction of insulin signaling pathway in old animals, but cerebral ketone body metabolism is independent