# Prevalence and risk factors of behavioural changes associated with age-related cognitive impairment in geriatric dogs

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# PREVALENCE AND RISK FACTORS OF BEHAVIOURAL CHANGES ASSOCIATED WITH AGE-RELATED COGNITIVE IMPAIRMENT IN GERIATRIC DOGS

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## Introduction

Ageing is generally associated with a decline in a range of cognitive functions. In human beings, dementia has been defined as a general mental deterioration or global decline of intellectual ability sufficient to produce functional disability (Hensel 1990). Dementia is typically characterized by both memory loss and decline in other cognitive functions such as behavioural disturbances and interference with normal daily functioning (Knopman 1998).

Senior dogs often suffer a decline in cognitive function, which involves memory, learning, perception and awareness (Landsberg and Araujo 2005). Common age-related behavioural problems include a reduction in the dog attention and activity, inability to navigate stairs, wandering and disorientation, disturbance of the sleep-wake cycle, lose housetraining habits, reduced interaction with people and other animals and decreased exploratory behaviour (Siwak and others 2002). When this range of behavioural problems, that involve deficits in memory and learning, are not caused by any medical condition (Manteca 1997, Heath 2002), they are identified by practicing veterinarians as the cognitive dysfunction syndrome (CDS).

Cognitive impairments reflect neuronal, neurotransmitter, metabolic, cerebrovascular or biochemical degenerative changes in brain (Ruehl and others 1995). A distinctive feature of the CDS is the extensive β-amyloid peptide deposition within the neurones and at the synaptic regions of the dog brain (Satou and others 1997, Borrás and others 1999). These deposits are similar to the primitive or early stage β-amyloid plaques in the brains of human patients with Alzheimer's disease (AD) (Cummings and others 1993, 1996a). Indeed, the deposition of such plaques in the cerebral cortex and hippocampus is significantly correlated to the cognitive decline (Head and others 1998, Colle and others 2000). Although neurofibrillary tangles are not present in aged dogs, canine CDS has been proposed as a good model for AD, because

neuropathologic and behavioural changes are comparable between both pathologies (Ruehl and others 1995, Cumming and others 1996b).

Previous studies realised in the USA showed that the prevalence of behavioural changes associated with age-related cognitive impairment is high (Nielson and others 2001), that is age dependent (Bain and others 2001) and influenced by reproductive status (Hart 2001). However, prevalence of age-related behavioural impairment is frequently subestimated because many owners assume that these problems are an inherent and untreatable result of age (Landsberg 2002), and because CDS has only been recently considered as a disease of senior dogs (Landsberg and Araujo 2005). A presumptive diagnosis of CDS can be made only when age-related behavioural changes are identified in the absence of any underlying medical cause, since brain biopsy and histopathologic examination are not diagnostic options (Heath 2002).

Although there is not a successful treatment that can cure CDS, the symptoms could be delayed with diet, behavioural and pharmacological treatment (Ruehl and others 1995, Heath 2002). Therefore, owners should identify any signs of cognitive impairment as early as possible. This could be best accomplished by providing dog owners with a list of behavioural signs to consider, and should be advised to report any behavioural change to their veterinarian (Landsberg 2005).

The aim of the study was to assess the prevalence of age-related behavioural changes in a randomly selected population of senior dogs receiving veterinary care. In addition, information was collected about sex, reproductive status, body weight and age, in order to identify possible risk factors.

## Materials and Methods

### Selection of cases

Records of veterinary clinics from Valencia and Zaragoza (Spain) were reviewed to identify cases of geriatric dogs. A total of 4476 cases were reviewed of which 573 (12.8%) were older than nine-year-old. The sample size required was determined according to population size, expected prevalence (50%) and desidered level of confidence (99%). Finally, 325 animals

were included and all of them were receiving veterinary care. Dogs with medical problems that could induce similar signs to cognitive impairment were excluded.

Dog population was balanced according to sex (50.5% females and 49.5% males). Neutered animals represented 18.2% of the population (67.7% females and 33.3% males). Dogs were classified as “small breed” (≤ 15kg) and “medium-large breed” (>15kg). According to this, 42.2% and 57.8% of the animals weighted ≤ 15kg and >15kg, respectively. Finally, the number of animals included in the study decreased with age being 56%, 37.5% and 6.5%, 9-11, 12-14 and 15-17 years old, respectively.

**Interview and assessment**

In the absence of any definitive diagnostic test in vivo, diagnosis for age-related cognitive impairment is based on the recognition of any sign related to four behavioural categories – sleep/wake cycles, social interaction, learning and house training and signs of disorientation (Table 1)–, without other behavioural and medical dysfunctions.

It was used a phone interview adapted from the study of Nielson and others (2001) which include an open-ended question related to behavioural categories. Clinical records were reviewed and owners were asked whether the dogs had any medical problems not apparent from the hospital records, especially vision or audition dysfunction. They were also asked about feeding, mobility alterations and eventual medication.

A behavioural category was considered to be impaired if neither it had been observed when the dog was younger nor a medical explanation existed. According to the severity of the signs, cognitive impairment was classified into mild (one impaired category), moderate (two impaired categories) or severe (three or four impaired categories).

**Statistical analysis**

A stratified case-cohort design was applied. The prevalence of age-related cognitive impairment was calculated within the sample population according to sex, reproductive status, weight and age. In addition, the distribution of cases in the different behavioural categories was considered. The differences in the frequency of cognitive impairment cases within sex, neutering, weight and age were assessed by Chi-square test ($p<0.05$). Data were analysed with the SPSS 12.0 computer software (SPSS, Inc. Chicago. USA). Risk factors associated with

age-related cognitive impairment were analyzed studying the Relative Risk (RR) and its Confidence Interval (CI) adjusted for sex, neutering, weight and age by using the epidemiological program Win Episcope 2.0. (Thrusfield et al., 2001).

**Results**

The results of our statistical analysis showed that 22.5% of the inquired geriatric dog population had one or more behavioural categories impaired (Figure 1.a). Females were significantly more affected (Figure 1.b) and had more risk of developing age-related cognitive impairment than males (RR: 2; CI: 1.2-3.1). The prevalence of cognitive impairment in neutered dogs was significantly higher than in intact ones (Figure 1.c). Furthermore, neutered dogs had more risk than intact ones (RR: 1.9; CI: 1.2-2.9). Results showed that there were significant differences between dogs according to their weight. Accordingly, small dogs showed significantly higher prevalence (Figure 1.d) and an increased risk of showing age-related cognitive impairment than large dogs (RR: 1.7; CI: 1.1-2.9). Concerning the severity of behavioural changes, 14.1% of the sample population suffered mild cognitive impairment, 6.2% moderate and only 2.2% of the study population suffered severe cognitive impairment (Figure 1.a).

As expected, the prevalence of cognitive impairment showed a significant increase with dogs age (Figure 2). Accordingly, only 14.8% of the younger dogs analyzed were affected by any sign of cognitive impairment (0% of them severe), but the prevalence increased to 29.5% of the 12-14-year-old animals (3.3% severe), and to 47.6% of the 15-17-year-old population (14.3% severe). Similarly, elder dogs had more risk of presenting any sign than younger animals (RR: 3.2; CI: 1.8-5.6).

Finally, the most impaired behavioural categories were social interaction (37.7%) and learning and house training (37.7%), followed by changes in sleep/wake cycles (20.2%) and disorientation (16.4%).

**Discussion**

This study confirms that cognitive impairment is clearly an age-related process in dogs. Our results are in accordance with a previous study conducted in the USA (Nielson and others

2001), although a greater prevalence of cognitive impairment among the elder dogs was described (68% in dogs between 15 and 16-year-old). In human AD, age is also a risk factor (Mangone 2002) which onset usually after 65 years old and the incidence doubles every 5 years (WHO 2006). According to our results, the severity of cognitive impairment related behaviours are also positively related to the dogs' age. A study had also demonstrated that age-related behavioural changes are progressive in dogs (Bain and others 2001), and marked memory deficits occur by the age of 12 (Studzinski and others 2006).

To our knowledge, this is the first time that risk factors associated with sex and age-related cognitive impairment behaviours are asserted in dogs. According to the risk factor assessment, female dogs are a major risk group within geriatric dogs' population. Likewise, women have increased risk of developing AD, which may suggest the existence of hormone-mediated process more than genetic factors (Mangone 2002), or else be due to the greater longevity of females (WHO 2006). Endogenous sex hormones affect cognition through an initial organisational role in the perinatal period and during the adult life, and they could be possibly helpful in the prevention of dementia (Barrett-Connor and others 1999, Kandel and others 2000). In human beings, several studies have suggested that high serum levels of estradiol and testosterone in women and men respectively, are related to a better cognitive capacity (Barrett-Connor and others 1999, Manly and others 2000, Yaffe and others 2000, Yaffe and others 2002, Moffat and others 2002, Wolf and Kirschbaum 2002). A decrease in serum estradiol concentration has also been observed in women with AD (Manly and others 2000), and hence hormone replacement therapies have been proposed to treat AD (Barrett-Connor and others 1999, Manly and others 2000). Recently, benefit of estrogen treatment on cognition has also been described in aged monkeys (Hao and others 2007). The role of gonadal hormones is also supported by the differences between neutered and intact dogs, found in the present study. In this regard, neutered dogs showed almost twice the risk of developing age-related cognitive impairments in comparison with intact dogs. Hart (2001) had already suggested that the presence of circulating testosterone in aging sexually intact male dogs might slow the progression of cognitive impairment, and that estrogens would be expected to have a similar protective role.

The present results indicate that small breeds have significantly greater prevalence of age-related behavioural changes than medium and large breeds. This may be due to the greated longevity of small breed dogs (Nielson and others 2001). Indeed, large breed dogs tend to die younger, presumably as a consequence of quicker ageing in the cardiovascular, musculoskeletal and endocrine system (Patronek and others 1997).

The most impaired behavioural categories are social interaction and house training. This latter is also one of the most frequent owner complaints (Chapman and Voith 1990). The four behavioural categories evaluated in this study are considered as CDS indicators involving learning and memory (Heath 2002). The presence of amyloid deposits in the cortex and hippocampus in the brains of dogs affected by CDS are related to the lost of these cognitive capacities (Head and others 1998).

The results of this study suggest that practicing veterinarians should take into account age-related cognitive impairments, since they affect more than 20% of dog geriatric population. In the same way, practitioners should consider that neutered and small breed dogs have more risk to develop age-related behavioural changes, especially those related to house-training and social interaction.



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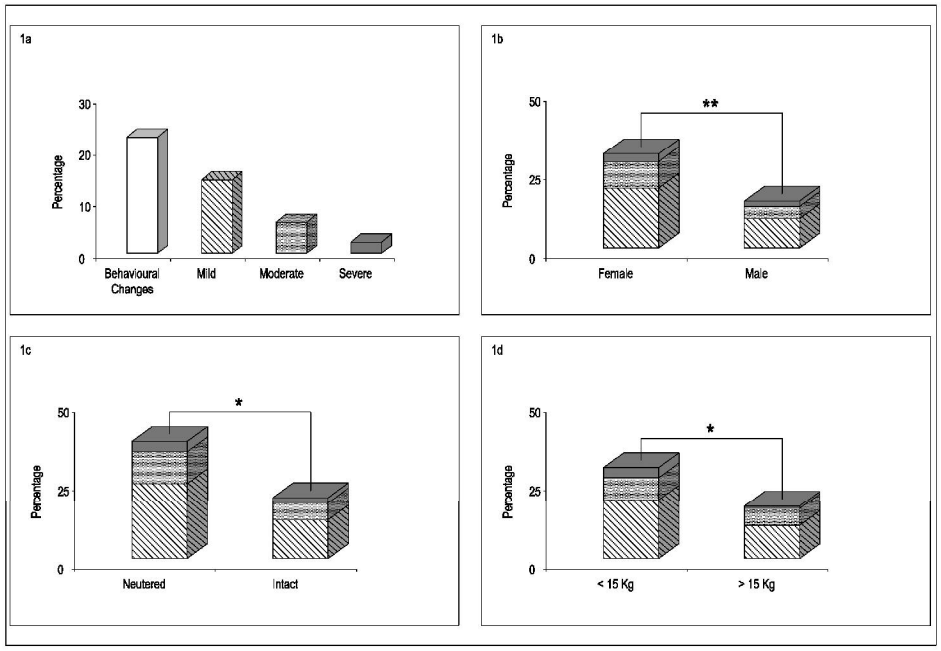
**Legends**

**Table 1.** Signs of the four behavioural categories that addressed cognitive dysfunction.

**Figure 1.** (a) Prevalence of age-related behavioural changes in senior dogs (b) in relation to sex, (c) reproductive status, (d) and body weight. Asterisks indicate significant differences after Chi-square test. *:p<0.05, **:p<0.01.

**Figure 2.** Prevalence of age-related cognitive impairment signs in senior dogs in relation to age and severity of the syndrome. Asterisks indicate significant differences after Chi-square test. **:p<0.01.

| Category | Behavioural signs |
|---|---|
| **Sleep/wake cycles** | |
| | Walks or barks at night<br>Changes in sleeping time<br>Altered activity level |
| **Social Interaction** | |
| | Decreases greeting behaviour<br>Does not look for owners attention<br>Does not recognise familiar people<br>Does not play with owner or other animals<br>Decreases responsiveness to stimuli |
| **Learning and house training** | |
| | House soiling<br>Forgets known commands or tricks<br>Deficits in learning and memory |
| **Disorientation** | |
| | Gets lost in familiar locations<br>Does not know to go out of narrow places<br>Goes to wrong side of door<br>Eyes fixed on the horizon |




**(a) Prevalence of age-related behavioural changes in senior dogs (b) in relation to sex, (c) reproductive status, (d) and body weight. Asterisks indicate significant differences after Chi-square test. *:p<0.05, **:p<0.01**

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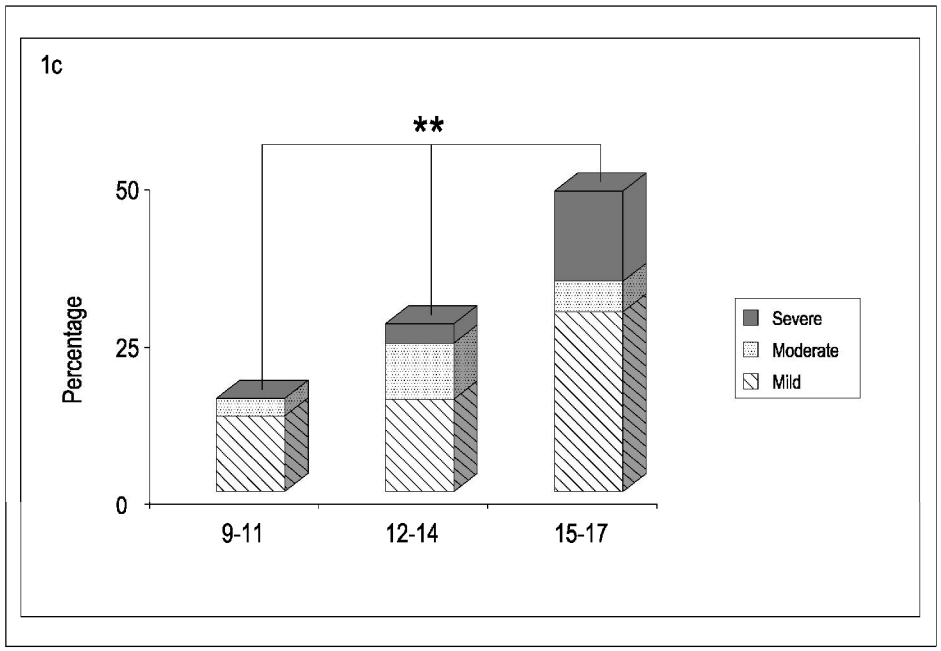


**Prevalence of age-related cognitive impairment signs in senior dogs in relation to age and severity of the syndrome. Asterisks indicate significant differences after Chi-square test. **:p<0.01.**

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