

## APPARENT SENILITY IN GERIATRIC CATS

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With improvements in nutrition and veterinary medicine the life expectancy of pet cats is increasing; there are now more elderly cats than ever before. In USA over the last 10 years, there has been a 15% increase in cats over 10 years of age, and in the UK it is estimated that there are currently ~ 2.5 million 'senior' cats. Since this accounts for ~30% of the pet cat population the good management of these individuals is becoming an ever more important consideration for small animal veterinary practitioners.

Unfortunately, accompanying this growing geriatric population there are increasing numbers of pets with signs of altered behaviour and apparent senility. These behavioural changes may result from many different disorders (Figure 1) including systemic illness (e.g. hyperthyroidism), organic brain disease (e.g. a brain tumour), true behavioural problems (e.g. separation anxiety), or cognitive dysfunction. Diagnosis involves a full investigation looking for underlying illness (Figure 2) and assessment for behavioural problems. Once these have been ruled out cognitive dysfunction syndrome (CDS) should be considered, although, ante-mortem, this is a diagnosis of exclusion. **The most commonly seen changes include spatial or temporal disorientation, altered interaction with the family, changes in sleep-wake cycles, house-soiling with inappropriate urination/defecation, changes in activity, and/or inappropriate vocalisation (often displayed as loud crying at night)** (Figure 3).

Cognitive dysfunction syndrome is a term that is applied to age-related deterioration of cognitive abilities, characterised by behavioural changes (as described above), where no medical cause can be found. **Recent studies suggest that as many as 28% of pet cats aged 11–14 years develop at least one geriatric-onset behaviour problem, and this increases to over 50% for cats of 15 years of age or older.**

The cause of the syndrome is still unknown, but i) compromised cerebral blood flow and ii) chronic free radical damage are both believed to be important. i) Numerous vascular changes can occur in the brain of old cats, including a decrease in cerebral blood flow, the presence of small haemorrhages around the blood vessels, and a form of arteriosclerosis. In addition, the brain of an elderly cat may also be subject to compromised blood flow and hypoxia due to heart disease, anaemia, blood clotting defects, or underlying hypertension. ii) A small amount of the oxygen that is used by cells in normal energy production is normally converted to free radicals. As cells age they become less efficient, producing less energy and more free radicals. (As a simile think of increasing emissions as a car engine ages and becomes less efficient). Normally, these free radicals are removed by the body's natural antioxidant defences, including a number of special enzymes and free radical scavengers, such as vitamins A, C and E. The balance between the production and removal of free radicals can be upset by disease, age, and stress. An excess of free radicals can lead to damage and the brain is particularly susceptible because it has a high fat content, a high demand for oxygen, and a limited ability to repair. Ultimately, chronic damage can eventually lead to disease processes similar to those seen in humans suffering from Alzheimer's disease (AD), with alteration of proteins within nerve cells (e.g. tau hyperphosphorylation) and deposition of protein plaques (made from  $\beta$ -amyloid protein) outside the nerve cells.

### Management of cats with CDS

While there are no published studies relating to the treatment of cats with CDS it is possible to consider potential treatment options by extrapolation from studies of humans with AD and dogs with CDS. Potential interventions therefore include dietary modification, environmental management, and drug therapies.

- *Dietary modification and environmental management*

Diets enriched with antioxidants and other supportive compounds (e.g. vitamin E, beta carotene, and essential fatty acids) are believed to reduce oxidative damage, so reducing  $\beta$ -amyloid production, and improving cognitive function. In humans, studies have shown that high intake of fruits, vegetables, vitamins E and/or C, folate and/or B<sub>12</sub> may improve cognition (although excessive intake of some of these compounds can have harmful effect). In addition, alpha-lipoic acid and l-carnitine enhance mitochondrial function, and

omega-3 fatty acids promote cell membrane health and have, in humans, been found to be beneficial in the treatment of dementia. In general, combinations of these compounds are believed to work best.

There have been a number of studies investigating the potential benefit of various supplements in dogs with CDS. For example, a study of dogs over six years of age, when given a supplement containing omega-3 fish oils, vitamins E and C, L-carnitine, alpha-lipoic acid, coenzyme Q, phosphatidylserine and selenium (this supplement is sold in the UK as Aktivait® from VetPlus) over a two month period resulted in significant improvements in signs of disorientation, social interaction, and house soiling. Unfortunately, a different formula is needed for cats as alpha-lipoic acid is toxic in this species so products containing it should not be given. While the new feline-safe version of Aktivait is on the market, trials in cats still need to determine its efficacy.

Environmental enrichment can lead to an increase in nerve growth factors, the growth and survival of nerves and an increase in cognitive function. The combination of environmental stimulation (e.g. toys, company, interaction, and food hunting games) and a diet enriched with antioxidants is believed to have a synergistic action in improving cognitive function. In aged dogs, a four year study on the use of an antioxidant-enriched diet (e.g. vitamins E and C, selenium, fruit and vegetable extract [beta carotene, other carotenoids, flavinoids]), mitochondrial cofactors (dl-lipoic acid and l-carnitine), and essential fatty acids (omega-3 fatty acids) (Hill's b/d®), plus environmental enrichment (e.g. toys, kennel mate, walks, and cognitive experience testing) revealed rapid (2-8 weeks into treatment) and significant improvements in learning and memory. Interestingly, while there was no reversal of existing pathology, the antioxidants did appear to prevent the deposition of more  $\beta$ -amyloid while the environmental enrichment did not.

While a similar study showing improvement of CDS in cats in response to dietary supplementation is not yet available, a five year study feeding healthy old cats (7-17 years old; n=90) a diet (Nestlé Purina Pro Plan Age 7+®) supplemented with antioxidants (vitamin E and  $\beta$ -carotene), essential fatty acids (omega-3 and 6 fatty acids) and dried whole chicory root (which contains the prebiotic inulin to modify intestinal flora) resulted in the supplemented cats living significantly longer (and more healthily) than the un-supplemented ones. Other similarly supplemented diets are now on the market (e.g. Hill's Feline j/d which is actually designed for cats with arthritis – it is supplemented with a mixture of anti-oxidants [e.g. vitamins C and E, and beta carotene], essential fatty acids, chondroprotectants [e.g. methionine, glycosaminoglycans, glucosamine, and chondroitin sulphate], and L-carnitine and lysine [to aid obesity management and the build-up of lean muscle]: in a two month study of 75 cats of 12 years of age or older, that were not selected for signs of CDS or (osteoarthritis), where owners were asked to complete questionnaires >70% improved in one or more signs of cognitive function (and >50% improved in one or more signs of mobility).

Unfortunately, once cats develop significant clinical signs of CDS, instigating environmental change can actually have a negative effect. This is because affected cats often become very stressed and cope poorly with change; whether in their environment, their daily routine, their diet, or the members of the household. The cat's response to this stress is to show more obvious signs of CDS (e.g. anorexia, hiding, and/or upset of toileting habits). For these cats, where possible, change should be kept to a minimum, and when it cannot be avoided it should be made slowly and with much reassurance. Some cats may become so demented and cope so poorly with change that they may benefit from having their area of access reduced in size (e.g. to a single room containing everything they need); this core territory can then be kept safe and constant. Environmental application of synthetic feline appeasement pheromone (Feliway®; Ceva) can also help in reducing feline anxiety.

- *Potential drug therapies*

There are a growing number of possible drug options for AD. These include various cholinesterase inhibitors (to increase the availability of acetyl choline at the neuronal synapses), selegiline (to manipulate the monoaminergic system), antioxidants (e.g. Vitamin E), and non-steroidal anti-inflammatory drugs (to reduce neuronal damage). While **there are no drugs licensed for the treatment of CDS in cats**, selegiline, propentofylline and nicergoline have all been used in this species with varying degrees of success (see below). Other drugs that have been used to treat particular signs of CDS in cats include anxiolytic drugs, such as buspirone and benzodiazepines (e.g. diazepam/Valium - although hepatotoxicity is a particular risk with this drug), or antidepressants (that lack anticholinergic effects) such as fluoxetine.

As yet there are no drugs licensed for the treatment of CDS in cats, and no drugs that have been proven to work in the treatment of CDS in this species. However, a number of drugs have been used 'off label'. These include selegiline (Selgian®; Ceva: suggested dose 0.25-1.0 mg/kg PO q24h), propentofylline (Vivitonin®; Intervet: suggested dose 12.5 mg/cat PO q24h) and nicergoline (Fitergol®; Merial: suggested dose quarter of a 5mg q24h), all of which have been used in cat with varying degrees of success, e.g. a small open trial using selegiline showed a positive effect and the American Association of Feline Practitioners supports the use of this drug for the treatment of CDS.

**Figure 1: Potential causes of behavioural changes in geriatric cats:**

- Arthritis (the pain and/or dysfunction of arthritis is often under-recognised in elderly cats)\*.
- Systemic hypertension (high blood pressure may either be primary or secondary to hyperthyroidism, renal failure, diabetes mellitus, acromegaly or hyperadrenocorticism)
- Hyperthyroidism
- Chronic kidney disease
- Diabetes mellitus
- Urinary tract infection
- Gastrointestinal disease
- Liver disease
- Neurological defects (either sensory or motor deficits)
- Reduced vision or hearing
- Brain tumours (e.g. lymphoma, meningioma)
- Infectious disease (e.g. FIV, FeLV, toxoplasmosis, FIP)
- Dental or periodontal disease
- Inflammatory disease in general
- Pain in general
- True behavioural problems
- Cognitive dysfunction syndrome

\* The importance of arthritis should not be overlooked. Radiographic evidence of degenerative joint disease is present in 70-90% of cats over 10 years of age. Associated pain and/or dysfunction can result in reduced activity and mobility, aggression, altered interactions with the family, and/or loss of litter box training. When asked, most owners list the diseases that they see in their older cats in a different order to the list generated by veterinary surgeons. Top of the owner's list is arthritis, and this is followed by kidney failure, deafness, blindness, hyperthyroidism, bronchitis, and dental problems (V Halls, personal communication, 2002). Owners can help their arthritic cats by adjusting their house; for example, by moving food and water bowls to lower surfaces, adding ramps to allow easier access to favoured sleeping areas, providing deep comfortable bedding that will support and protect the cat's joints (heated beds can be particularly soothing), and placing low-sided litter boxes within easy cat reach.

**Figure 2: Initial investigation of behavioural changes in geriatric cats should include:**

- Full history, including the possibility of previous trauma (which may have lead to arthritis), any potential exposure to toxins or drugs, and any recent environmental changes (in the household, family members, diet, etc.). Asking specific questions about alternations in the cat’s behaviour can help in determining how the cat has changes (see **Mobility / Cognitive Dysfunction Questionnaire**).
- Full physical examination (including assessment of body weight, body condition score, retinal examination and a full neurological examination).
- **Assess systemic blood pressure** (this is particularly important as hypertension occurs commonly in older cats and cat many of the same signs as CDS)
- Assess haematology and serum biochemistry, including thyroid hormone level
- Urine analysis (including urine protein to creatinine ratio and bacterial culture)
- **Further investigation may include:**
- Where appropriate, serological testing for FeLV, FIV, Toxoplasmosis or FIP
- Thoracic, abdominal or skeletal radiography, abdominal ultrasound examination, ECG, echocardiography, intestinal endoscopy / exploratory laparotomy and biopsy collection, as indicated from initial findings.
- Head CT or MRI

<b>Mobility / Cognitive Dysfunction Questionnaire*</b>			
	<b>Yes</b>	<b>Maybe</b>	<b>No</b>
My cat is less willing to jump up or down	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
My cat will only jump up or down from lower heights	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
My cat shows signs of being stiff at times	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Overall my cat is less agile than previously	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
My cat shows signs of lameness or limping	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
My cat has difficulty getting in or out of the cat flap	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
My cat has difficulty going up or down stairs	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
My cat has more accidents outside the litter tray	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
My cat spends less time grooming	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
My cat is more reluctant to interact with me	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
My cat plays with other animals or toys less	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
My cat sleeps more and/or is less active	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
My cat cries out loudly for no apparent reason	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
My cat appears forgetful	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

\*Ensure there have been no environmental reasons for the change.

It can be difficult to differentiate between many of the changes caused by CDS and those caused osteoarthritis. Indeed, the two conditions often occur concurrently in old cats and many of the treatments for one condition also help the other. Anyone wanting more information about osteoarthritis should contact the author and ask for her notes on the subject: [Danielle.Gunn-Moore@ed.ac.uk](mailto:Danielle.Gunn-Moore@ed.ac.uk).

**Figure 3: Behavioural changes that can be seen in geriatric cats and may be associated with cognitive dysfunction syndrome (CDS):**

- Spatial disorientation or confusion, e.g. getting trapped in corners or forgetting the location of the litter box (house-soiling is the most common reason for referral of old cats to behaviouralists)
- Altered social relationships, either with their owners or other pets in the household e.g. increased attention seeking or aggression
- Altered behavioural responses e.g. increased irritability or anxiety, or decreased response to stimuli
- Changes in sleep/wake patterns
- Inappropriate vocalisation e.g. loud crying at night
- Altered learning and memory, such as forgetting commands or breaking housetraining
- Changes in activity e.g. aimless wandering or pacing, or reduced activity
- Altered interest in food, either increased or, more typically, decreased
- Decreased grooming
- Temporal disorientation e.g. forgetting that they have just been fed

## Clinical case of cognitive dysfunction

**History:** Max, a 14 year old neutered male Manx cat was presented for routine examination and vaccination. He was an indoor/outdoor cat and the only pet in the household. His owner mentioned Max had developed several behavioural changes, including becoming less independent, and crying more for attention and food. He had shown occasional head tremors and was refusing to eat dry food.

**Physical examination:** Max had become slightly thin, had significant dental disease and his coat was matted. No other abnormalities were noted.

### **Diagnostic evaluation and initial treatment:**

Haematology was unremarkable, serum biochemistry revealed a mild elevation in urea (total thyroxin level was within normal limits); urinalysis revealed a specific gravity of 1.030 (indicating that Max had a mild degree of kidney damage). Tests for FeLV and FIV test were negative.

A dental examination was performed and four teeth were extracted. On recheck one month later the head tremors had resolved and he was eating dry food again.

### **Follow-up:**

One year later, Max was refusing dry food again. His was vocalising more, and he was noticeably more clingy while generally having lower overall activity levels.

Investigations revealed that his kidney damaged was a little worse than before. Systemic blood pressure was normal. A dental examination and full mouth radiographs were performed; no more teeth had to be removed. A canned kidney support diet was recommended, although it was stressed that if Max refused to eat this, he was to be offered his normal food in order to keep him from losing more weight.

Recheck 2 months later revealed that Max was disinterested in food, had little interest in going outside, was crying more and had been defecating on the bed. Tests showed that there were no further changes in this kidney function and his blood pressure was still in the normal range. His owner was considering euthanasia. However, the vet thought that Max may have cognitive dysfunction syndrome (geriatric senility) so they suggested that he be fed any food he was interested in and started him on treatment with selegiline (Selgian in UK, Anipryl in US, at 2.5 mg every 24 hours to be given in the morning). Environmental enrichment was also discussed, including providing Max with more mental stimulation by spending time each day engaged in play sessions using various cat toys, cardboard boxes and paper bags. Because of the house soiling, litter box changes were also considered. Because Max was showing signs of arthritis, a litter box with lower edges was recommended and an additional litter box was to be added. Initially, the extra litter box was to be filled with sand-like cat litter. If Max preferred the 'foot feel' of this new litter it was then to be introduced slowly to his other box. The litter boxes were to be regularly scooped and cleaned as kidney disease leads to the production of an increased volume of urine and therefore to more litter box soiling. The owner was also advised to not inadvertently reinforce unwanted behaviours, such as giving Max extra attention when he was whining and crying for attention.

At a 3 month recheck, Max's owner described Max to be much improved. He was not hiding as much and was more interested in his surroundings. His vocalizations had reduced and he appeared to be happier. The owner was much happier and felt that Max's quality of life was now good again.

Max's kidney disease progressed slowly over the following year. The owner started injecting him once a week with subcutaneous fluids, his blood pressure slowly climbed; requiring daily medication with amlodipine (Istin) and Max finally succumbed to an intestinal tumour nearly 3 years after first his vet had seen recognised cognitive impairment.

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