paw®
PURE ANIMAL WELLBEING
By BLACKMORES

MENTAL HEALTH

in Dogs & Cats

2024 edition for professional reference only

MENTAL HEALTH CONCERNS IN DOGS & CATS

Behaviour related problems in pets are one of the most common reasons for surrender to animal shelters.[1] Mental health concerns can often manifest in signs such as anxiety, aggression, inability to learn, and phobias, which can have a detrimental effect on the quality of life of pets, and their owners. [2]

Some owners may recognise that their pet is uneasy, and will report anxiety-related behaviours. Others may mistakenly believe that their anxious pet is stubborn, jealous, or vindictive. These owners may only report the problematic manifestations, such as night-time waking, destruction, or excessive vocalisation, without recognising these as clinical signs of an underlying mental health concern.[3]

DID YOU KNOW?

26% of dogs and **17%** of cats have general fearfulness

39% of dogs have a noise phobia

43% of dogs show some degree of aggressive behaviour

21% of cats are timid

18% of cats are hyperactive

Canine statistics obtained from a study surveying over 3000 dog owners.[9]
Feline statistics based on market research.[29]

WHY DO MENTAL HEALTH CONCERNS OCCUR IN PETS?

Mental health concerns, such as anxiety and fear, result from a complex interaction of:

- **Environmental conditions**
- **Genetics**
- **Neurological adaptation**
- **Conditioning**

Neurotransmitters, such as serotonin, influence how an animal responds to stressful situations. Occasional fear or anxiety may be appropriate in some contexts, but repeated overreactions to situations perceived as harmless can be detrimental for the pet, and the owner.[4]

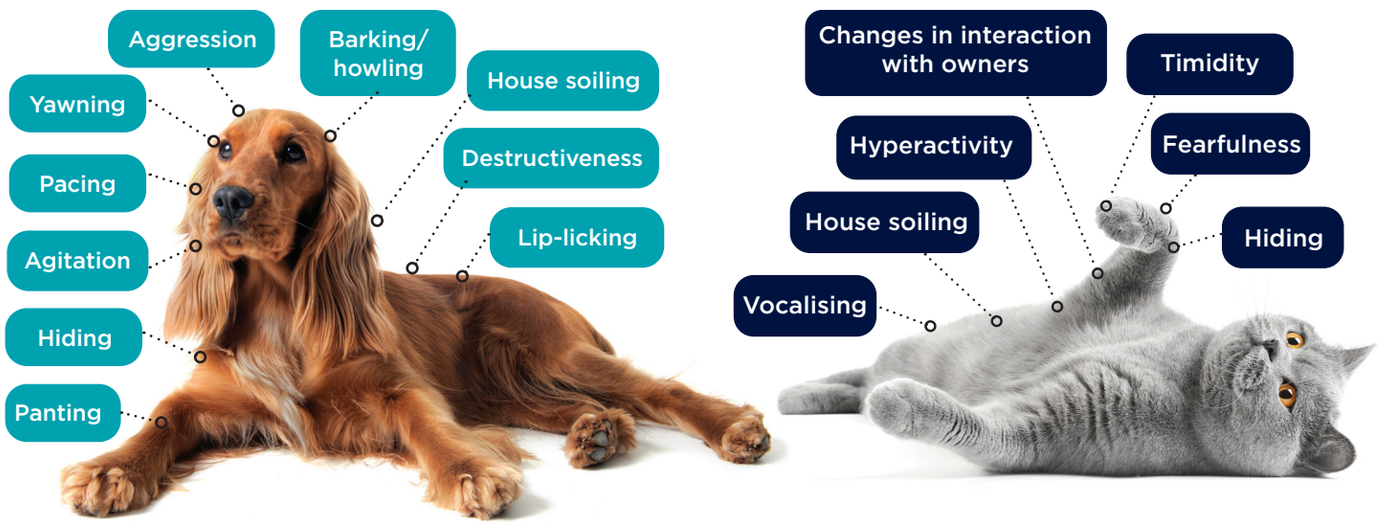
Conditions of the brain such as cognitive decline can manifest as changes in a pet's behaviour, resulting in signs of mental health concerns such as separation anxiety, and noise phobias.[5]

CATS ARE NOT JUST SMALL DOGS

Behaviour consultations are quite different in cats compared to dogs. A common error made by veterinarians is assuming that cats are just small dogs, and trying to apply the same treatment rules.[28]

By respecting their genuine ethology, considering their territory, predator and prey status, hierarchy, and social life, we can better understand feline behaviour.

MENTAL HEALTH CONCERNS 'ON THE OUTSIDE' [3, 4, 6, 29]

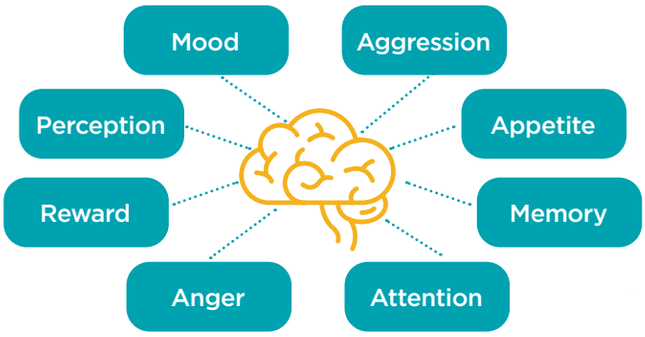


MULTI-MODAL APPROACH TO THE MANAGEMENT OF MENTAL HEALTH CONCERNS IN DOGS & CATS

1.	ENVIRONMENTAL MODIFICATION	Initially avoiding or removing the triggers for anxiety, fear, or other mental health concerns is often necessary to be able to progress towards behavioural therapy.[7]
2.	BEHAVIOURAL MODIFICATION	Employing behavioural therapies can help the pet to achieve a positive relationship with stimuli that would normally trigger a negative response. This can be done through controlled desensitisation, and the establishment of a stable predictable environment, and pet-owner routine.[8]
3.	ALTERNATIVE THERAPIES	Nutraceuticals such as L-tryptophan, SAMe, DHA, and other supplements, can play important roles in the management of mental health concerns - either as a primary therapy, or an adjunct to other therapies.
4.	PHARMACOLOGICAL THERAPIES	Some pets may require pharmacological intervention for the treatment of their mental health concerns, and to facilitate learning. These are often administered in the short-term, but may be required long-term in advanced cases.

SEROTONIN AND THE CENTRAL NERVOUS SYSTEM

In the central nervous system (CNS) of humans and animals, serotonin (5-hydroxytryptamine, 5-HT) serves as a neurotransmitter.[10,11] Despite the relatively low concentration of brain-derived serotonin compared to that in the rest of the body, it has a broad impact. It is vital in the regulation of many behavioural and neuropsychological processes including:[12]



L-TRYPTOPHAN: THE PRECURSOR TO SEROTONIN

L-tryptophan is an essential amino acid found in many protein-based foods, such as meat, dairy, fruits and seeds.[13] Of all the amino acids in the body, it is found in the lowest concentrations.[13] L-tryptophan is the sole precursor of peripherally and centrally produced serotonin.[6] Only 3% of dietary tryptophan is used for serotonin synthesis throughout the body, and it is estimated that only 1% of dietary tryptophan is used for serotonin synthesis in the brain.[14]

L-TRYPTOPHAN

↓ **Tryptophan hydroxylase***

L-5-HYDROXY TRYPTOPHAN

↓ **L-aromatic amino acid decarboxylase**

5-HYDROXYTRYPTAMINE (SEROTONIN)

* Hydroxylase pathway is the rate limiting step due to its limited distribution and low affinity for other amino acids.[8]

L-TRYPTOPHAN SUPPLEMENTATION AND ITS ANXIOLYTIC EFFECT ON MULTI-HOUSED CATS[30]

In a double-blinded placebo-controlled study, a total of 25 multi-housed cats were observed. Cats were randomly assigned, with half of the group receiving dietary supplementation of L-tryptophan (L-trp) starting on the 7th week, whilst the other half received a placebo product. The daily dose of L-trp was 12.5 mg/kg administered at mealtime.

Cats were observed 5 days per week during a period of three and a half months (2 weeks for habituation, 4 weeks without supplementation, and 8 weeks with supplementation).

After L-trp supplementation, all the stereotypic vocalisation, agonistic, exploration, and sustaining behaviours decreased. In the same way, house soiling, scratching and agonistic interactions inside the group significantly decreased.

Stress-related behaviours including avoidance, threatening behaviour, fighting, displacement activity, staring, and vocalisation decreased significantly in cats supplemented with L-trp.

These results suggest that L-trp supplementation alters the frequency of stress related behaviours, and decreases anxiety signals in multi-housed cats.

Consequently, L-trp supplementation can be regarded as a valuable tool to assist in the treatment of some behavioural disorders in cats. As the L-trp supplementation reduces some of the animal's anxiety signs and stress-related behaviours, this suggests that it is also beneficial in improving their overall welfare.

L-TRYPTOPHAN TO IMPROVE MENTAL HEALTH AND ANIMAL WELFARE[15]

Behavioural responses associated with anxiety and stress are important welfare considerations. L-tryptophan supplementation can be a very efficient tool to help treat some behavioural disorders in animals as part of a multi-modal behaviour therapy plan.

In a double-blinded controlled study, 30 working dogs from the National Guard in Portugal were either supplemented with L-tryptophan, or a placebo product, to determine the therapeutic efficacy of L-tryptophan for improving signs of anxiety, and therefore welfare.

Dogs were observed during a period of 3.5 months (2 weeks for habituation, 4 weeks without supplementation, and 8 weeks with supplementation), 5 days a week. Following L-tryptophan supplementation, bark, stare and stereotypical behaviours decreased.

Tryptophan-supplemented, low-protein diets are associated with lower dominance aggression and territorial aggression behaviour scores in dogs.[16]

The study featured 11 dogs with dominance aggression, 11 dogs with territorial aggression, and 11 dogs with hyperactivity. Each group was fed four different diets for one week each, in a randomised order. Two diets had low protein content, whilst the other two had high protein content. Two of the diets (one low-protein and one high-protein), were supplemented with tryptophan. Owners scored their dog's behaviour daily by using customised behavioural scoring sheets.

Tryptophan-supplemented low-protein diets were associated with significantly lower behavioural scores than low-protein diets without tryptophan supplements (Figure 1). For dominance aggression, behavioural scores were highest in dogs fed the un-supplemented high-protein diet (Figure 2).

Therefore, for dogs with dominance aggression, the addition of tryptophan to high-protein diets, or alternatively, a transition to a low-protein diet, may aid in reducing aggression. For dogs with territorial aggression, tryptophan supplementation of a low-protein diet may be helpful in reducing aggression.

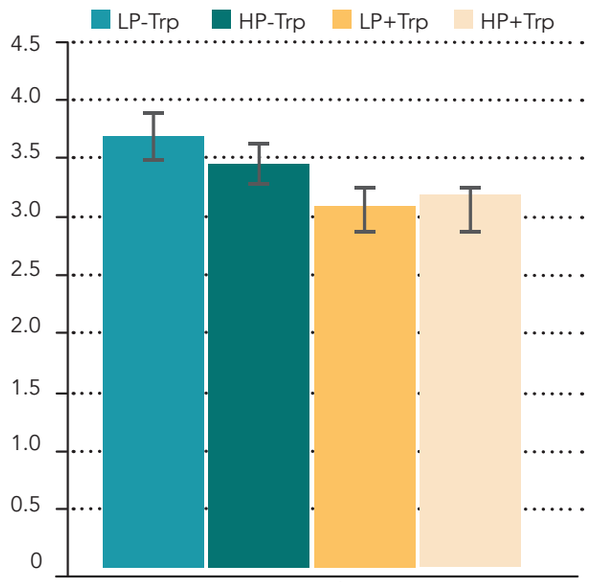


Figure 1. Mean daily territorial behaviour scores (±SE)

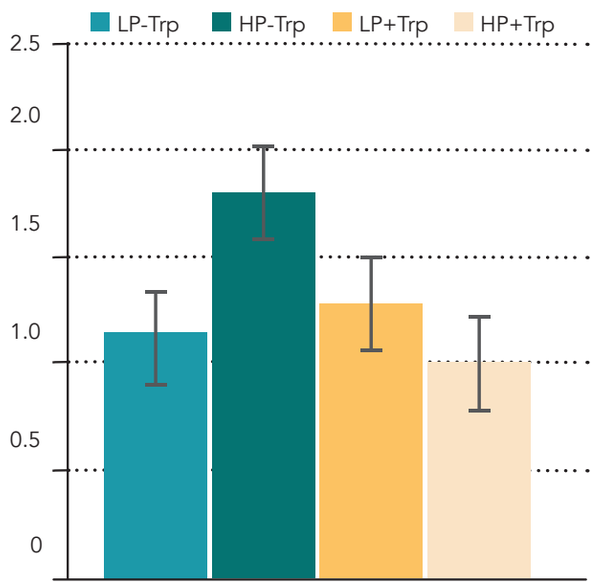


Figure 2. Mean daily dominance aggression behaviour scores (±SE)

CROSSING THE BLOOD-BRAIN-BARRIER

Boosting serotonin in the central nervous system with L-tryptophan

Serotonin is unable to cross the blood–brain barrier.[17] For brain-derived serotonin production to occur, tryptophan first needs to gain access to the central nervous system via the blood-brain barrier, where it is then converted to serotonin.[13]

Supplementing with serotonin therefore, is not an option to enhance serotonin levels in the central nervous system. Instead, supplementation with L-tryptophan-containing nutraceuticals, or tryptophan-rich dietary proteins, can enhance tryptophan availability to the brain, and boost brain-derived serotonin levels.

SUPPORTING HEALTHY BRAIN FUNCTION WITH ESSENTIAL FATTY ACIDS

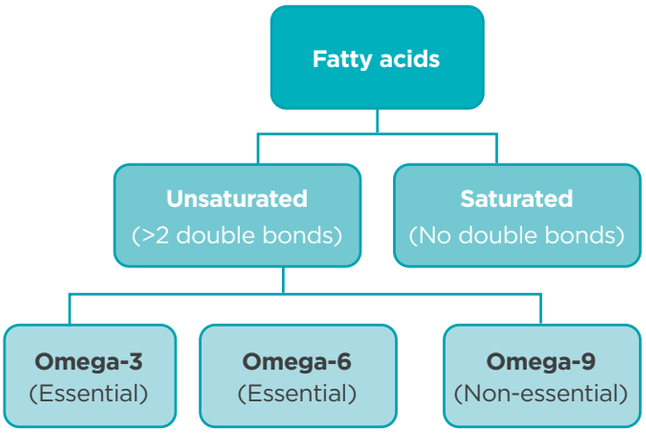
Omega-3 fatty acids eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) exhibit neuroprotective properties.[20] DHA is quantitatively the most important omega-3 fatty acid in the brain. Fatty fish (salmon, tuna, mackerel), and mammary milk, are all rich sources of DHA. Low amounts of this vital omega-3 fatty acid are also present in meat, and eggs.[21] DHA is essential for the growth, and functional development of the brain in young mammals, and is required for the maintenance of normal brain function in adults.[20] In humans, decreases in DHA in the brain are associated with age-related cognitive decline, and with the onset of sporadic Alzheimer's disease. A deficiency in DHA has also been correlated with depression in people.[21]

WHAT MAKES ESSENTIAL FATTY ACIDS ESSENTIAL?

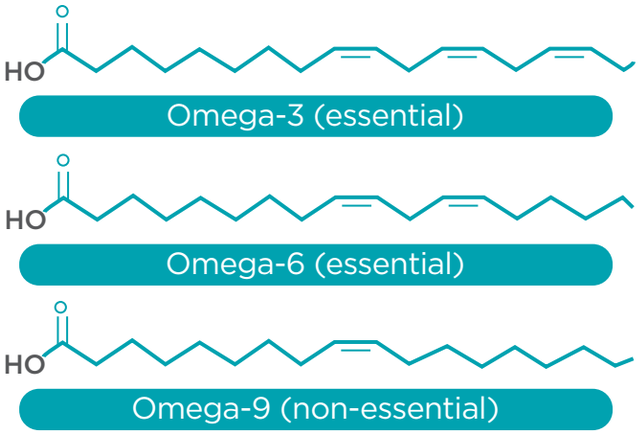
Omega-3 and omega-6 fatty acids are considered essential because dogs and cats are unable to synthesise them in sufficient quantities to meet their metabolic needs.[18]

Structurally, an EFA has at least two double bonds, and is named according to where these double bonds occur. This precise molecular configuration enables each individual fatty acid to fold upon itself three dimensionally, so that it can participate in cell membrane, and physiological events that are important for normal health.[18]

Classification of fatty acids



Structural differences between the various fatty acids



FUNCTIONS OF FATS AND FATTY ACIDS[19]

Fat, and essential fatty acids have many important functions in the body including:

- The provision of energy
- Aiding in fat-soluble vitamin absorption
- Modulating inflammation
- Acting as a precursor to eicosanoids and prostaglandins
- Serving structural roles as a key component of cell membranes
- Promoting healthy growth and development
- Contributing to optimal skin and coat health

DID YOU KNOW?

Not all EFA supplements are equal[19]

The most efficient way to increase EPA and DHA in a pet's diet is to provide these fatty acids in a supplemental form, such as fish oil. When supplementing a diet with fatty acids, it is important to choose a quality supplement. The potential exists for nutrient excesses (mainly vitamins A and D), and toxin exposure, including mercury exposure with fish oil supplements. It's important therefore to take care when selecting a fish oil supplement. Ensure that it is sourced from a reputable company with good quality control practices.

Improved cognition, memory, and psychomotor functions in puppies fed a diet rich in fish-derived DHA.[22]

Forty-eight Beagle puppies were divided into three groups post-weaning, and received one of three foods: low-DHA, moderate-DHA, or high-DHA food as their sole source of nutrition, from eight weeks until 12 months of age.

Visual discrimination, learning and memory tasks, psychomotor performance tasks, and physiological tests were performed at various time points.

The high-DHA group had significantly better results for reversal task learning, visual contrast discrimination, and early psychomotor performance in side-to-side navigation through an obstacle-containing maze than did the moderate-DHA, and low-DHA groups.

The study showed that dietary fortification with fish oils rich in DHA following weaning improved cognitive, memory, psychomotor, immunologic, and retinal functions in growing dogs.

Fortification of a complex food with concentrations of specific nutrients in greater than the minimum daily recommended amounts, may enhance specific physiological outcomes in healthy, growing puppies.

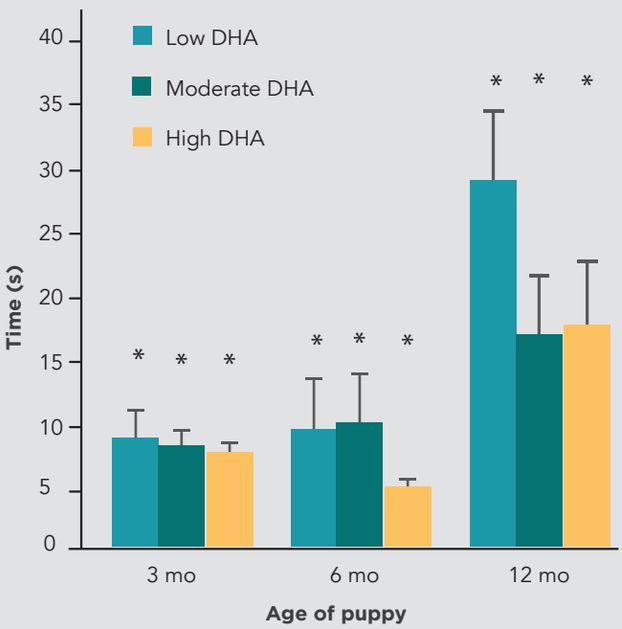


Figure 3. Mean + SD time for psychomotor task completion.

* Within a certain time period, values with asterisks indicate a significant difference between the groups.

DIETARY ENRICHMENT WITH DHA FOR DOGS WITH COGNITIVE DECLINE[23]

A randomised, double-blinded, controlled clinical trial was conducted to evaluate the effects of dietary enrichment with antioxidants, mitochondrial cofactors, and DHA in dogs with cognitive dysfunction over a 60 day period. 125 pet dogs ≥ 7 years of age, that were consistently recognised by their owners as having at least two behavioural characteristics of age-related cognitive decline, were evaluated. Half of the dogs were assigned to receive an enriched diet, whilst the other half were assigned the control diet.

Significant improvements were found for 14 out of 16 behavioural attributes for the enriched-diet group, versus only 4 out of 16 for the control group. Furthermore, significant advancements at day 60 were seen in agility, recognition of family members, and recognition of other animals for the enriched-diet group.

COGNITIVE DYSFUNCTION IN SENIOR PETS

Thanks to continuous improvements and advancements in veterinary care, our pets are now fortunately living longer than ever. Therefore, the need to understand, and to provide the tailored support required to address health issues that arise with senior pets, including mental health issues, is of particular importance.[24]

PREVALENCE OF COGNITIVE DYSFUNCTION SYNDROME IN SENIOR DOGS[24]

of dogs aged 10-12 years[1]

of dogs aged 12-14 years[1]

of dogs aged 14+ years[1]

THE PATHOPHYSIOLOGY OF COGNITIVE DECLINE

Cognitive Dysfunction Syndrome (CDS) is a chronic and progressive disease.[25] Several pathophysiological changes occur in the brains of animals with CDS, some of which are visible during post mortem examination. One key change is that the brain mass and cell numbers progressively decrease, whilst the ventricular size increases. Simultaneously, the meninges fibrose, and the white matter degenerates.

Similar to humans with Alzheimer's disease, there is an accumulation of β-amyloid plaques in the brains of CDS-affected dogs.[24,26] These plaques accumulate in the cerebral cortex and the hippocampus, interfering with nerve conduction. Other changes include alterations in the activity of various neurotransmitters, including serotonin, dopamine, acetylcholine, and norepinephrine.[1]

In human Alzheimer patients, reductions of S-adenosylmethionine (SAMe) concentrations are found in the cerebrospinal fluid (CSF), and in several areas of the brain in these patients, which is an important consideration for our animal patients.[26]

Dogs with CDS suffer a decline in memory, learning, perception, and awareness. [6] Changes observed by owners typically fall into several broad categories, including changes in activity, sleep, appetite, and social interaction.[24] Cognitive changes may occur suddenly, but are generally gradual in onset.[24]

WHAT DOES COGNITIVE DECLINE LOOK LIKE?[26]

S-ADENOSYLMETHIONINE AND COGNITIVE DYSFUNCTION

S-adenosylmethionine (SAMe) is an endogenous molecule formed from methionine, and adenosine triphosphate (ATP) in every living cell. SAMe is particularly abundant in the brain and the liver, which serves as the major site of systemic SAMe synthesis.[31]

Methylation plays an important role in maintaining the fluidity and integrity of cell membranes. SAMe-dependent methylation reactions are also required to synthesise neurotransmitter monoamines such as serotonin, dopamine, adrenaline, noradrenaline, and histamine.[2] Demethylated SAMe is metabolised to glutathione, the most abundant and important intracellular antioxidant in the body, which protects tissues against free radical damage.[26] Treatment with SAMe reportedly stimulates brain glutathione, thereby reducing oxidative stress, which is increased and strongly implicated in age related cognitive dysfunction.[32]

SAMe biochemical pathways[27]

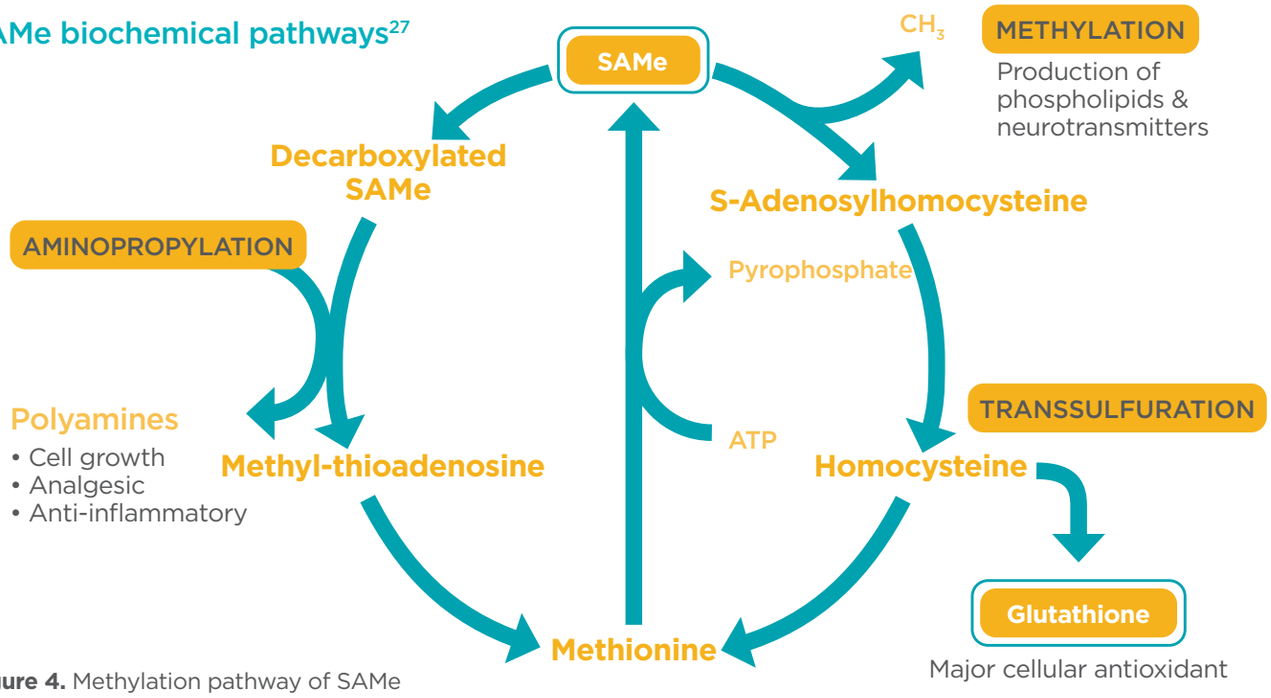


Figure 4. Methylation pathway of SAMe

SAMe reduces age-related mental decline in dogs[26]

A randomised, double-blinded, placebo-controlled clinical field trial at five veterinary centres in France, Belgium, and Spain was conducted to determine if oral SAMe supplementation could be useful in the management of cognitive dysfunction in 36 senior dogs.

Seventeen dogs were administered SAMe PO once daily at a mean dose of 18.5 mg/kg, whereas the remaining 19 dogs received placebo tablets according to an identical treatment regimen for a total of two months. Clinical and behavioural evaluations were performed at baseline, and then again after four and eight weeks of treatment.

Compared with the placebo group, SAMe supplemented dogs showed a significant improvement in activity and awareness scores (attention to surroundings). Eight out of the 12 behavioural parameters (including disorientation, confusion, learning deficits, change in the sleep-wake cycle, and anxiety, amongst others) improved with SAMe supplementation over the study period, compared to 3 out of the 12 parameters in the placebo group.

SAMe supplementation provided a fair to good improvement in geriatric behaviour signs in about three-quarters of the cases at eight weeks, resulting in an improved quality of life.

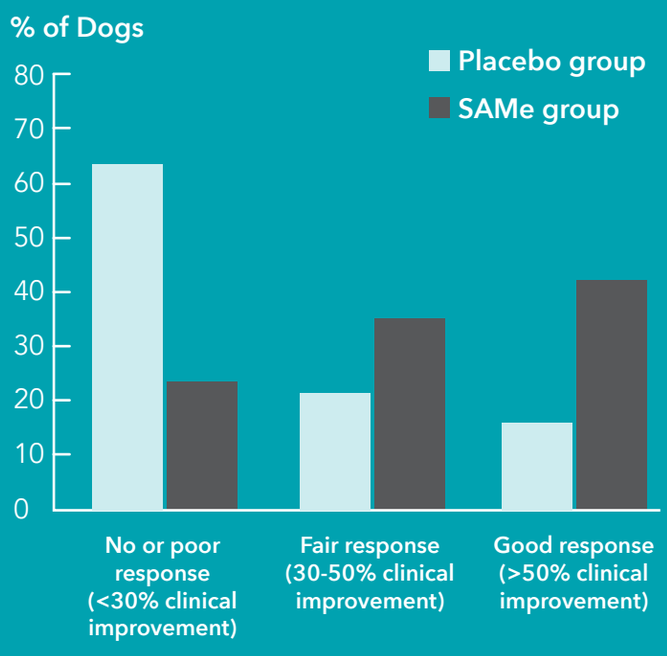


Figure 5. Overall response to treatment as measured on day 60.

CHOOSING THE RIGHT PAW PRODUCT FOR YOUR PATIENTS

SUPPLEMENTATION WITH L-TRYPTOPHAN

PAW Complete Calm

Benefits:

- Contains high levels of tryptophan, a serotonin precursor, which may aid in reducing the signs of stress and anxiety.
- Contains B group vitamins (including B1, B5 and B6) to help support healthy nervous system function.
- Provides key vitamins and minerals to help maintain a healthy immune system.
- Contains DHA to support cognitive health.
- Tasty fish and chickpea chew format for ease of daily administration.

Each PAW Complete Calm chew contains:

Active ingredients	Cat chews (1.2g/chew)	Small Dog chews (2.5 g/chew)	Medium-large Dog chews (5g/chew)
Tryptophan	45.23 mg	90 mg	180 mg
Pantothenic acid (B5)	0.13 mg	1.57 mg	3.14 mg
Thiamine (B1)	0.13 mg	0.23 mg	0.45 mg
Pyridoxine (B6)	0.05 mg	0.145 mg	0.29 mg

Dosage:

Complete Calm for Cats dosage	
Size: 75 g tub (approx. 63 chews)	
Body weight	**Daily dose**
1 - 4.9 kg	2 chews
5 - 10 kg	4 chews

Complete Calm Small Dog dosage	
Size: 75 g tub (approx. 30 chews)	
Body weight	**Daily dose**
1 - 4.9 kg	½ a chew
5 - 9.9 kg	1 chew
10 - 15 kg	1 ½ chews

Complete Calm Medium-large Dog dosage	
Size: 300 g tub (approx. 60 chews)	
Body weight	**Daily dose**
1 - 4.9 kg	½ a chew
5 - 14.9 kg	1 chew
15 - 29.9 kg	2 chews
30+ kg	3 chews

Administration: Feed daily with food. The chews can be given whole or crumbled over food.

Storage: Store below 30°C.

Warnings/ Safety:

- For animal consumption only.
- Do not use if your cat is on behavioural medication.

Please read the label and follow the directions for use.

SUPPLEMENTATION WITH DHA

PAW Fish Oil 500: Veterinary strength

- Rich in omega-3 fatty acids, EPA & DHA to maintain optimal health, and wellbeing in dogs.
- Provides support for joint, skin, heart, kidney and bowel health.
- Sustainably sourced, and rigorously tested to Blackmores quality and purity standards.
- Formulated with EPA/DHA ratios (55:45) recommended for dogs based on nutritional standards published by the National Research Council, USA.

Key ingredients/0.5ml (1 pump = 0.5ml):

- Eicosapentaenoic acid (EPA): 275mg
- Docosahexaenoic acid (DHA): 225mg

Size: 200ml pump bottle.

Dosage:

Clinical indication for use	Daily dose (per 10 kg dog body weight)
Osteoarthritis	7 pumps
Renal disease	4 pumps
Atopic dermatitis, IBD, cardiovascular disease, idiopathic hyperlipidaemia	3 pumps
Maintenance	1 pump every second day

Warnings/prescribing information: Fish oil is generally safe and well tolerated. The NRC safe upper limit is 370 mg/kg$^{0.75}$.The most commonly expected adverse events are mild, self-limiting gastrointestinal signs. Other uncommon or rare side effects may include platelet inhibition, delayed wound healing, weight gain, and altered immune function. Consider discontinuing high doses for 2-3 weeks prior to and following surgery. Hyperglycaemia is a potential adverse effect, and caution should be used in diabetic patients receiving insulin concurrently. Store below 25° (air conditioning). Protect from light & store in a dry place.

SUPPLEMENTATION WITH SAMe

PAW HepatoAdvanced®

Benefits:

- Convenient, palatable tablet containing a blend of bioavailable antioxidants
- Provides detoxification support in the management of canine and feline liver disease by enhancing glutathione production
- Supports cognitive function in dogs

Active ingredients	Cat & Small Dog	Medium & Large Dog
S-Adenosyl-L-methionine disulfate p-toluenesulfonate (Equivalent to SAMe)	50 mg	310 mg
D-alpha tocopherol succinate (Vitamin E)	45 IU	200 IU
Silybin phospholipids Equivalent to silybin phosphatidylcholine (Equivalent to silybin A+B)	13 mg	90 mg

Size: 60 palatable tablets (Cat and Small Dog), 30 palatable tablets (Medium and Large Dog)

Dosing Chart		
Weight Range	**Cat & Small Dog**	**Medium & Large Dog**
1 – 2.4 kg	1 palatable tablet	
2.5 - 9.9 kg	2 palatable tablets	
10 – 14.9 kg	3 palatable tablets	½ palatable tablet
15 – 29.9 kg		1 palatable tablet
30 - 59.9 kg		2 palatable tablets*

Warnings/prescribing information: *DO NOT exceed 2 palatable tablets per day. **For optimal absorption, administer HepatoAdvanced® (as per the dosing chart above), once a day on an empty stomach.** For animal use only. For veterinary supply only. Store below 25°C in a dry place away from sunlight. Use with caution in pregnant or lactating animals as safe use has not been established in this population. SAMe has a wide safety margin. Side effects or overdose effects are rare, but are limited to mild gastrointestinal signs, immediate post pill nausea, and food refusal.[3,4] Concomitant use of SAMe with tramadol, meperidine, dextromethorphan, pentazocine, MAOIs (selegiline), SSRIs (fluoxetine), and other anti-depressants (amitriptyline, clomipramine) may theoretically cause additive serotonergic effects. Use with caution simultaneously.[30] Silymarin typically has no side effects, but consider drug interactions in polymedicated patients, such as the following: antiviral drugs, drugs affected by cytochrome P450 & CYP3A4 inhibition, and drugs cleared via hepatic glucuronidation. There are no commonly noted toxic effects derived from vitamin E supplementation, although it may inhibit the absorption of other fat- soluble vitamins when administered at high doses. Therefore, it is recommended to not exceed a total daily dose of 400IU per dog. [4, 5,10, 34] Vitamin E is not recommended in liver disease patients with evidence of vitamin K deficiency.[10]

Introducing the PAW Practitioner Range

Developed for vets, by vets.

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