paw®
PURE ANIMAL WELLBEING
By BLACKMORES

MENTAL HEALTH

IN DOGS

2022 edition for professional reference only

MENTAL HEALTH CONCERNS IN DOGS

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 & 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 worried and will report anxiety-related behaviours. Others may inaccurately believe their anxious pet is stubborn, jealous, or vindictive. These owners may only report the problematic manifestations, such as night-time waking, destruction, or excessive vocalization, without recognizing these as clinical signs of underlying mental health concerns.[3]

DID YOU KNOW?

In a study surveying over 3000 dog owners[9]:

26%
of dogs had general fearfulness

39%
of dogs had noise phobia

18%
of dogs had separation anxiety

43%
of dogs showed some level of aggressive behaviour

WHY DO MENTAL HEALTH CONCERNS OCCUR IN PETS?

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

environmental conditions

conditioning

neurological adaptation

genetics

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]

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

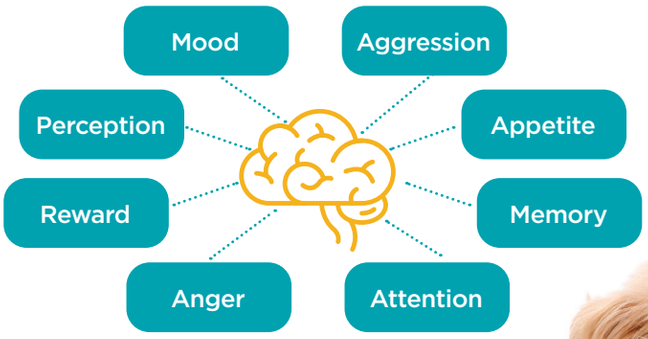
MULTI-MODAL APPROACH TO THE MANAGEMENT OF MENTAL HEALTH CONCERNS IN DOGS & CATS

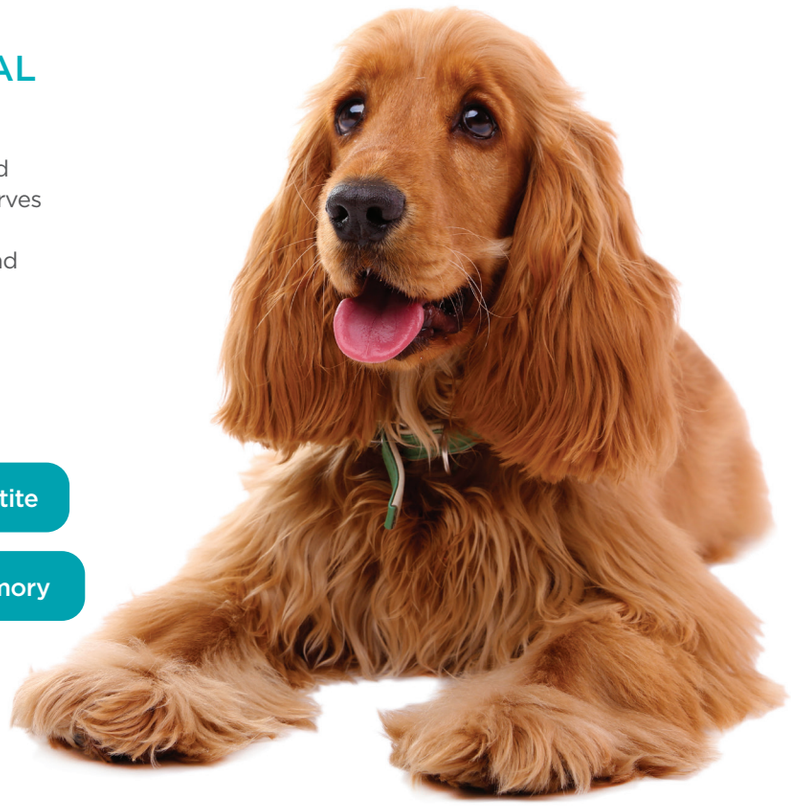
1.	ENVIRONMENTAL MODIFICATION	**Minimise exposure to evoking stimuli**	Initially avoiding or removing triggers for anxiety, fear or other mental health concerns is often necessary to be able to progress towards behavioural therapy.[7]
2.	BEHAVIOURAL MODIFICATION	**Help them cope with evoking stimuli**	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 desensitization, establishment of a stable, predictable environment and pet-owner routine.[8]
3.	ALTERNATIVE THERAPIES	**A gentle approach to managing mild to moderate cases.**[8]	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	**May be required for more advanced cases**	Some pets may require pharmacologic 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] Brain-derived serotonin is important in the regulation of many behavioural and neuropsychological processes.[12]

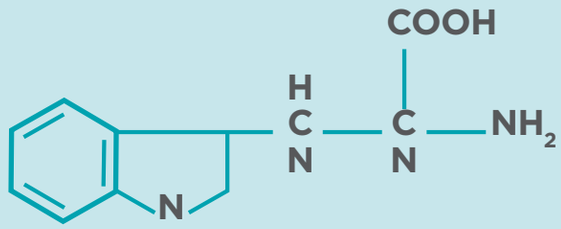
Brain-derived serotonin helps regulate[12]:





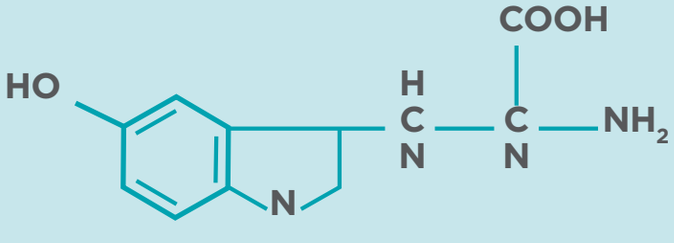
L-TRYPTOPHAN: THE PRECURSOR TO SEROTONIN

L-tryptophan is an essential amino acid found in many protein-based foods and dietary proteins including meats, dairy, fruits and seeds.[13] It is found in the lowest concentrations among the amino acids in the body.[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]



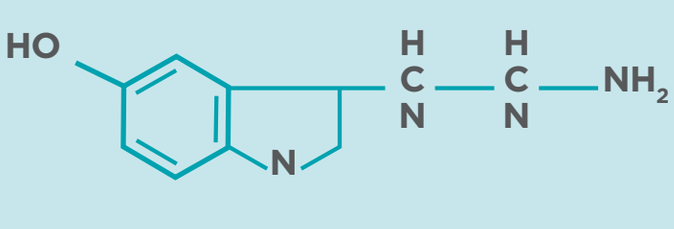
L-TRYPTOPHAN

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



Tryptophan hydroxylase

L-5-HYDROXY TRYPTOPHAN



L-aromatic amino acid decarboxylase

L-5-HYDROXY TRYPTOPHAN (SEROTONIN)

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-blind controlled study, 30 working dogs from the National Guard in Portugal were either supplemented with L-tryptophan or a placebo 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 per week. After L-tryptophan supplementation, bark, stare and stereotypical behaviours decreased.

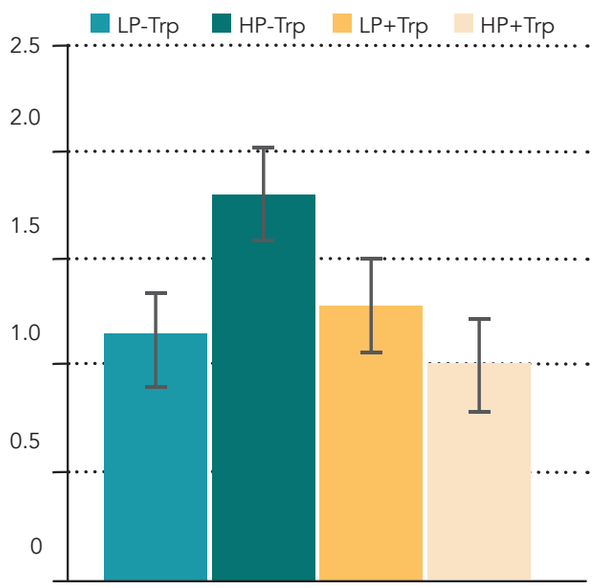
Tryptophan-supplemented, low-protein diets are associated with lower dominance aggression and territorial aggression behaviour scores in dogs.[16]

11 dogs with dominance aggression, 11 dogs with territorial aggression, and 11 dogs with hyperactivity were included. In each group, 4 diets were fed for one week each in random order. Two diets had low protein content and two diets 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 score sheets.

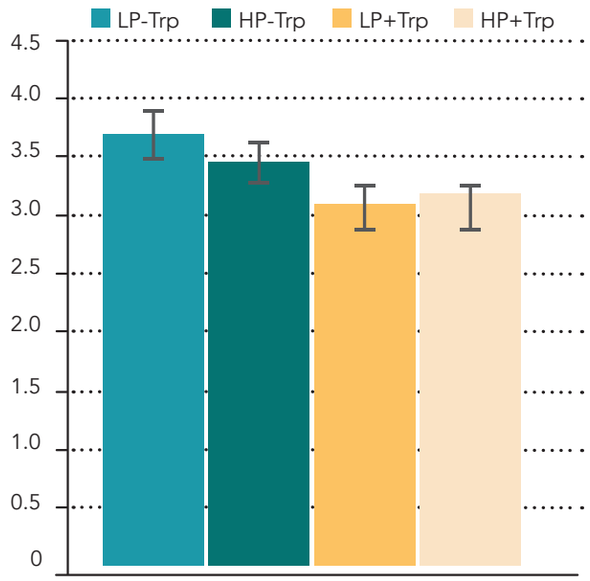
Tryptophan-supplemented low-protein diets were associated with significantly lower behavioural scores than low-protein diets without tryptophan supplements (Graph 2). For dominance aggression, behavioural scores were highest in dogs fed un-supplemented high-protein rations (Graph 1).

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

Graph 1: Mean daily dominance aggression behaviour scores (±SE)



Graph 2: Mean daily territorial behaviour scores (±SE)



CROSSING THE BLOOD-BRAIN-BARRIER

Boosting central serotonin with L-tryptophan

Serotonin does not 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 synthesis. 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 present in high levels in fatty fish (salmon, tuna, mackerel) and mammary milk, and is present at low levels in meat and eggs.[21]

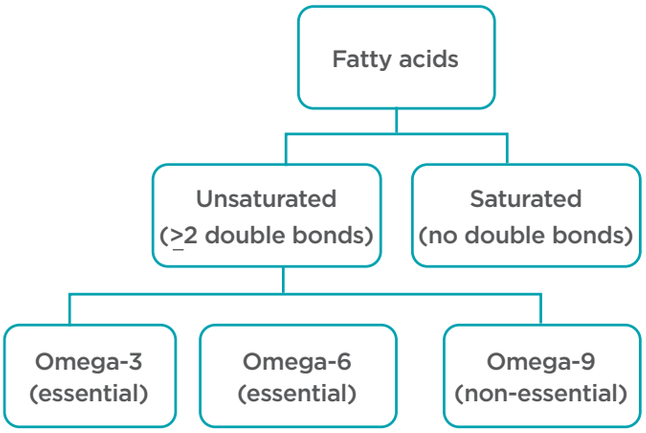
DHA is quantitatively the most important omega-3 fatty acid in the brain. DHA is essential for the growth and functional development of the brain in young mammals and is required for maintenance of normal brain function in adults.[20] In humans, decreases in DHA in the brain are associated with age-related cognitive decline and with the onset of sporadic Alzheimer's disease. A deficiency in DHA has been correlated with depression in people.[21]

WHAT MAKES ESSENTIAL FATTY ACIDS ESSENTIAL?

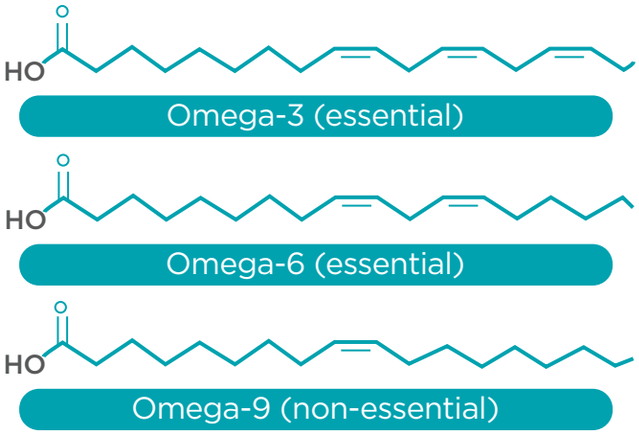
The essential nature of an essential fatty acid (EFA) is primarily due to an animals inability to synthesize it in sufficient quantities to meet its metabolic needs. Omega-3 and omega-6 fatty acids are considered essential.[18]

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

Classification of fatty acids



Structural differences between omega-3 fatty acids



FUNCTIONS OF FATS AND FATTY ACIDS[19]

The many functions of fat and essential fatty acids in the body include:

- Provide energy
- Aid in fat-soluble vitamin absorption
- Modulate inflammation
- Act as a precursor to eicosanoids and prostaglandins
- Serve structural roles as a component of cell membranes
- Promote healthy growth and development
- Affect skin and coat health.

DID YOU KNOW?

Quality control: 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. If supplementing a diet with fatty acids, it is important to choose a quality supplement. Potential exists for nutrient excess (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 that it is sourced from a reputable company with good quality control practices.

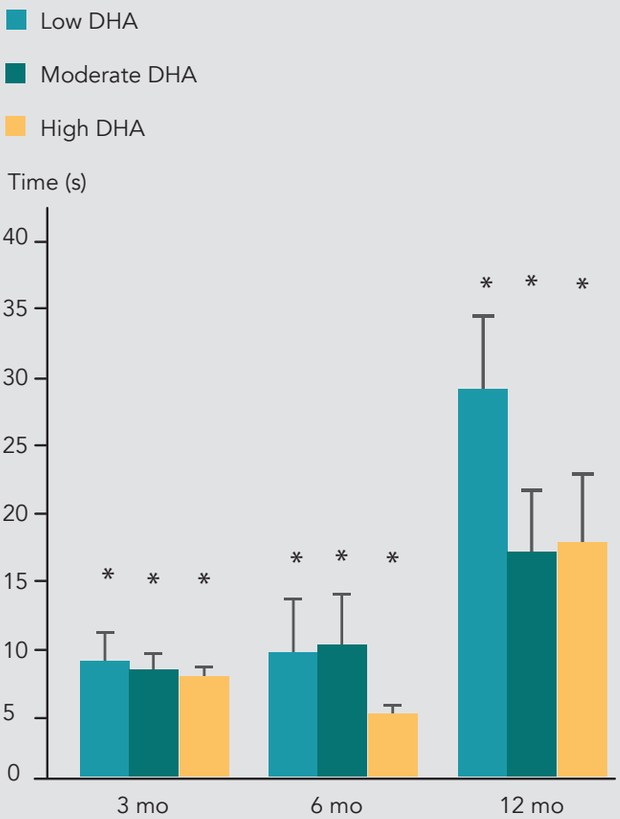
Improved cognition, memory and psychomotor functions in puppies fed a diet rich in fish-derived DHA.[22]

48 Beagle puppies were divided into three groups after 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 physiologic 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 greater than the minimum daily recommended amounts may enhance specific physiologic outcomes in healthy, growing puppies.



Mean + SD time for psychomotor task completion.
* Within a time period, values with asterisks are significantly different between groups.

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

A randomized, double- blinded, controlled clinical trial was conducted to evaluate 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 old that were consistently recognized 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 and half were assigned the control diet.

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

COGNITIVE DYSFUNCTION IN SENIOR PETS

Our pets are now considered a member of the family and fortunately, are living longer than ever thanks to continuous improvements and advancements in veterinary care. Therefore, the need to understand and address health issues that arise with senior pets, including mental health issues, is especially important.[24]

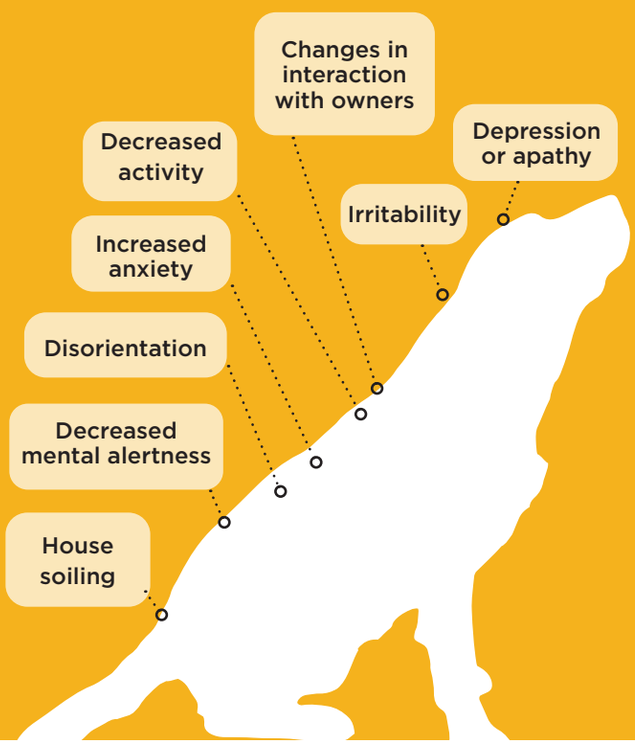
PREVALENCE OF COGNITIVE DYSFUNCTION SYNDROME IN SENIOR DOGS[24]

of dogs aged 10-12 years[1]

of dogs aged 12-14 years[1]

of dogs aged 14+ years old[1]

CLINICAL SIGNS COMMONLY ASSOCIATED WITH COGNITIVE DECLINE INCLUDE:[26]



THE PATHOPHYSIOLOGY OF COGNITIVE DECLINE

Cognitive Dysfunction Syndrome (CDS) is a chronic and progressive disease.[25] There are similarities between CDS and Alzheimer's disease in humans.[26] Several pathophysiologic changes occur in the brains of animals with CDS, some of which are visible during post mortem examination. For example, brain mass and cell numbers progressively decrease, while ventricle 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 dogs with CDS.[24,26] These plaques accumulate in the cerebral cortex and the hippocampus and interfere 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 usually gradual in onset.[24]

S-ADENOSYLMETHIONINE AND COGNITIVE DYSFUNCTION

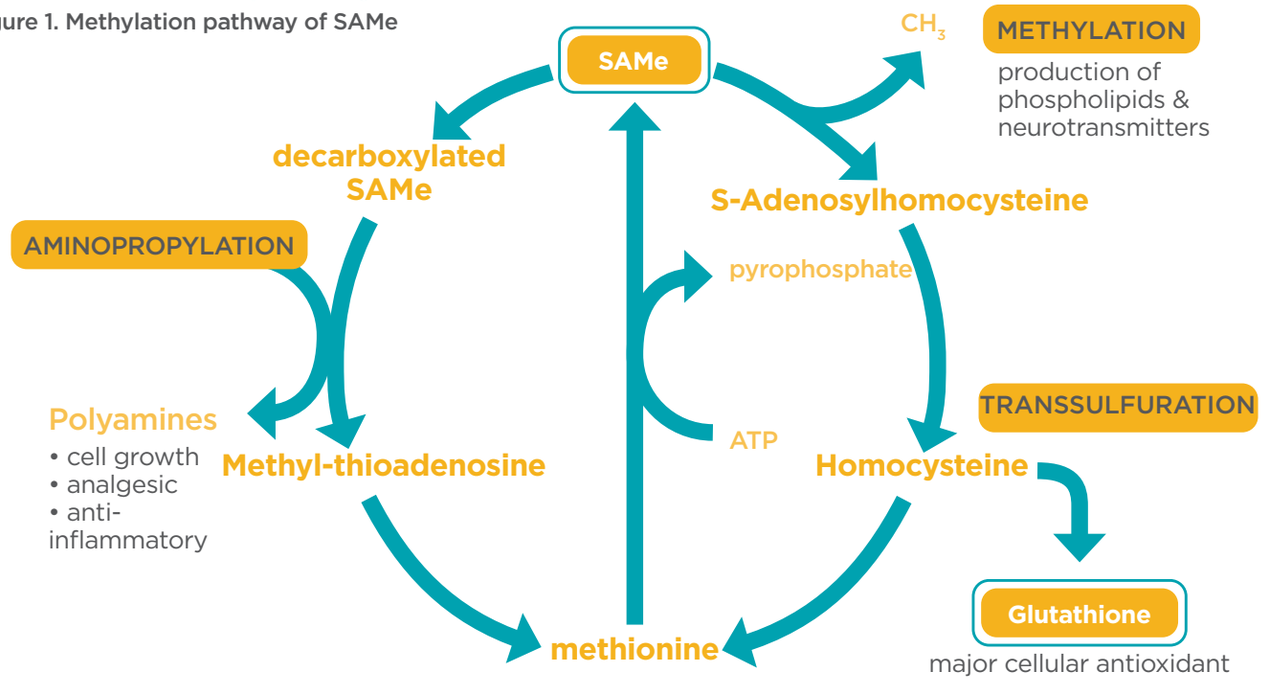
S-adenosylmethionine (SAMe) is an endogenous molecule formed from methionine and adenosine triphosphate (ATP) found in every living cell (Figure 1). SAMe is particularly abundant in the brain and liver. Several studies suggest that methyl group deficiency in the central nervous system may play a role in the aetiology of Alzheimer's disease in people.[26]

Methylation plays an important role in maintaining the fluidity and integrity of cell membranes. Demethylated SAMe is metabolised to glutathione, the main cell antioxidant that protects tissues against free radicals.[26]

SAMe-dependent methylation reactions are also required to synthesise neurotransmitter monoamines such as serotonin, dopamine, adrenaline, noradrenaline and histamine.[2]

SAMe biochemical pathway[27]

Figure 1. Methylation pathway of SAMe



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

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

Thirty-six dogs older than eight years were included in the study. To be included, at least two of the following signs related to old-age mental impairment had to be observed: disorientation, confusion, or learning deficits, decreased alertness or activity, decreased social interactions, change in the sleep-wake cycle, loss of housetraining; and anxiety.

Seventeen dogs were given SAMe orally once daily in tablet form (mean dose: 18.5 mg/kg) for two months. The other 19 dogs received identical placebo tablets according to the same treatment regimen. Clinical and behavioural evaluations were performed at baseline and then again after four and eight weeks of treatment.

Under the conditions of the study, SAMe tablets proved more effective than placebo in improving activity and awareness (attention to surroundings) in senior dogs, resulting in improved quality of life. Eight of the 12 behaviour parameters improved with SAMe supplementation over the study period, compared to three of 12 parameters in the placebo group (Figure 2). The symptomatic therapy was supportive, providing moderate to marked improvement of geriatric behaviour signs in about three-quarters of cases at eight weeks. The effects of the nutritional supplement seemed progressive over time, being significantly different from the control group between four and six weeks.

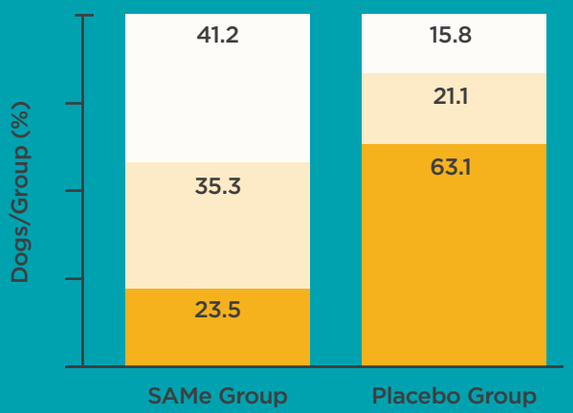


Figure 2. Percent reduction from baseline of the aggregate mental score of behavioural parameters, at week eight, in the SAMe vs placebo group.

CHOOSING THE RIGHT PAW PRODUCT FOR YOUR PATIENTS

Please read the label and follow the directions for use

SUPPLEMENTATION WITH L-TRYPTOPHAN

PAW Complete Calm Small Chews with tryptophan

Benefits:

- Contain tasty fish and chickpea protein
- Specifically designed for daily use in small dogs and may help alleviate signs of anxiety such as aggression
- Contain tryptophan & B group vitamins to help maintain nervous system function

Contains the following key ingredients in each 2.5g chew:

Tryptophan	90 mg
Pantothenic acid (B5)	1.57 mg
Thiamine (B1)	0.23 mg
Pyridoxine (B6)	0.145 mg

Dosage:

Weight (kg)	1-4.9 kg	5-9.9 kg	10-15 kg:
Daily Dosage	½ Chew	1 Chew	1 ½ Chews

Size: 60g Tub (Approx. 30 chews)

Storage: Store below 30°C.

Warnings/Safety: For animal use only.

PAW Complete Calm with tryptophan

Benefits:

- High levels of tryptophan to help relieve stress & anxiety.
- B group vitamins to help support healthy nervous function.
- Vitamins & minerals to help maintain a healthy immune system.

Contains the following key ingredients in each 5g chew:

Tryptophan	180 mg
Pantothenic acid (B5)	3.14 mg
Thiamine (B1)	0.45 mg
Pyridoxine (B6)	0.29 mg

Dosage:

Weight (kg)	1-4.9	5-14.9	15-29.9	30+
Daily Dosage	½ Chew	1 Chew	2 Chews	3 Chews

Size: 300g Tub (Approx. 60 chews)

Storage: Store below 30°C.

Warnings/Safety: For animal use only.

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.

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

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

Size: 200ml pump bottle.

Dosage:

Condition	Dosage
Osteoarthritis	Give 7 pumps per 10 kg per day
Renal disease	Give 4 pumps per 10 kg per day
Atopic dermatitis, IBD, cardiovascular disease, idiopathic hyperlipidaemia	Give 3 pumps per 10 kg per day
Maintenance	Give 1 pump per 10 kg every second day

Warnings/safety:

- 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

Benefits:

- Convenient, chewable 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

Key ingredients	Cat & Small Dog	Medium & Large Dog
(S) S-Adenosyl methionine disulfate tosylate (Equivalent to S- SAMe)	100 mg	310 mg
d-alpha-tocopheryl acid succinate (vitamin E)	90 IU	200 IU
Silybin/ phospholipids Equivalent to silybin phosphatidylcholine (Equivalent to silybin A+B)	26 mg	90 mg

Dosing Chart		
Weight Range	**Cat & Small Dog**	**Medium & Large Dog**
0 kg – 4.9 kg	½ chewable tablet	
5 kg - 9.9 kg	1 chewable tablet	
10 kg – 14.9 kg*	1 ½ chewable tablets	
15 kg – 29.9 kg		1 chewable tablet
30 kg +		2 chewable tablets*

For optimal absorption, administer Hepatoadvanced (as per the dosing chart above), once a day on an empty stomach.

Size: Each box contains 30 chewable tablets

Storage: Store below 25°C in a dry place away from sunlight

Warnings/Safety: *DO NOT exceed 2 chewable tablets per day. 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.[34] Concomitant use of SAMe with tramadol, meperidine, dextromethorphan, pentazocine, MAOIs (selegiline), SSRIs (fluoxetine), 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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