

FEEDING THE BRAIN:

PUTTING PURINA'S
NUTRITIONAL SCIENCE
INTO PRACTICE



HELPING PETS LIVE BETTER, LONGER LIVES

The Purina Institute is strongly committed to advancing nutritional science to benefit pet health. We represent a diverse, global team of more than 500 scientists and pet care experts — including nutritionists, veterinarians, behaviorists, molecular nutritionists, biochemists, microbiologists, and more — with a proven track record of making nutritional discoveries that improve the lives of pets around the globe.



WHY SHOULD YOU TALK ABOUT NUTRITION WITH YOUR CLIENTS?

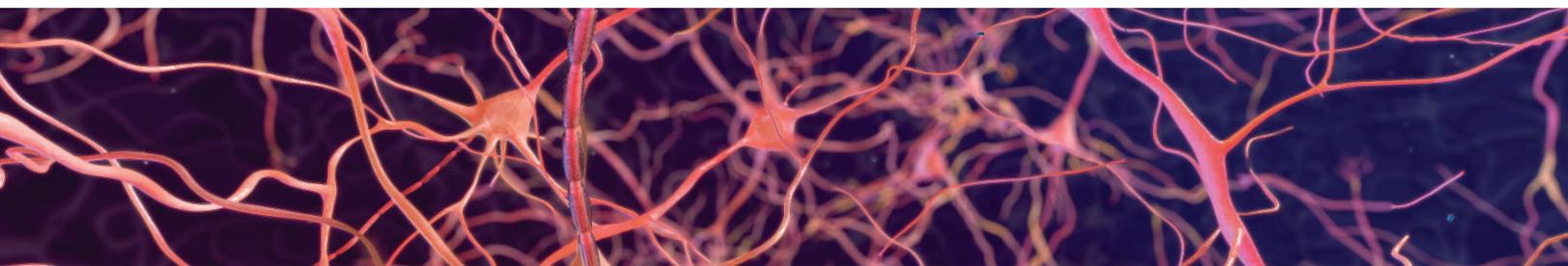
Nutrition can be a powerful adjunct to quality veterinary medicine, yet only 22% of veterinarians initiate nutrition conversations with their clients.¹ In the absence of credible advice from their veterinarians, pet owners may get conflicting information from a variety of sources (many of which are unreliable). If more veterinarians knew their clients trusted them to provide advice on pet nutrition, how would it change these conversations?

At the Purina Institute, we value the difference you're making to help pets live healthier lives. That's why we're collaborating with innovative pet care thinkers like you to elevate the topic of nutrition and take back the conversation.

On the following pages, you'll find clinically relevant learnings from more than a decade of Purina research on nutritional interventions for brain health. We've paired these findings with sample conversation starters that you can put into practice every day.

Find more clinically relevant learnings at PurinaInstitute.com.

¹ Source: Ipsos (2014). Vet Tracker US.



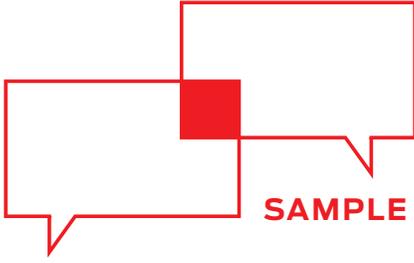
HOW AGE AND FEEDING SCHEDULE AFFECT BEHAVIOR

Purina scientists have advanced the study of canine and feline cognition by studying mental processing in the areas of learning, memory and attention to establish foundational knowledge and determine opportunities for intervention.

- Dogs have a circadian sleep/wake cycle, like humans, with higher levels of activity in the daytime than nighttime hours. Senior dogs still have circadian rhythms, despite reduced activity compared to adult dogs. *(Zanghi et al, 2008)*
- Similar to aged people, senior dogs are about 50% less active than early adult dogs; this may decrease their daily caloric needs and increase their risk of obesity unless their feeding is adjusted. *(Zanghi et al, 2012)*
- Senior dogs display alterations in nighttime sleep patterns, with more activity at night and earlier onset of daytime activity. *(Zanghi et al, 2012 and 2013)*
- Feeding dogs twice daily, as opposed to once daily, increases the dogs' awake time during the day by about 60 minutes and leads to a 20-30 minute earlier start to their days' activity. *(Zanghi et al, 2013)*
- Increased napping in dogs 11 years of age and older may be an early indicator of some memory loss. *(Zanghi et al, 2016)*
- Cognitive impairment may be present before behavioral signs are observed *(Zanghi et al, 2016)*, emphasizing the importance of preventive approaches to mitigate the risk factors for cognitive impairment.
- The areas in the brain responsible for memory appear to be at least partially independent from those responsible for learning and attention; if one type of memory or learning is affected, it doesn't necessarily mean that other functions are similarly affected. *(Zanghi et al, 2015)*

FEEDING DOGS TWICE DAILY,
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SAMPLE CONVERSATION STARTER:

“Now that your pet is approaching senior age [or is a senior], you can expect to see some changes in his/her activity level and possibly some changes in [his/her] sleep cycle – such as more frequent napping. Since [he/she] may be less active, we may need to adjust [his/her] food to prevent [him/her] from gaining weight that could make conditions like arthritis worse. If you’re not already feeding [him/her] twice daily, splitting [his/her] daily food into two feedings can help reduce the amount of change in activity and help keep [him/her] more active and healthy.”

PUBLISHED PURINA RESEARCH:

Zanghi, B. M., de Rivera, C., Araujo, J., & Milgram, N. W. (2008, November). Circadian sleep/wake patterns and cognitive performance in adult dogs change with age. Presented at Society of Neuroscience Conference, Washington, D. C.

Zanghi, B. M., Kerr, W., de Rivera, C., Araujo, J. A., & Milgram, N. W. (2012). Effect of age and feeding schedule on diurnal rest/activity rhythms in dogs. *Journal of Veterinary Behavior*, 7, 339-347. doi: 10.1016/j.jveb.2012.01.004

Zanghi, B. M., Kerr, W., Gierer, J., de Rivera, C., Araujo, J. A., & Milgram, N. W. (2013). Characterizing behavioral sleep using actigraphy in adult dogs of various ages fed once or twice daily. *Journal of Veterinary Behavior*, 8, 195-203. doi: 10.1016/j.jveb.2012.10.007

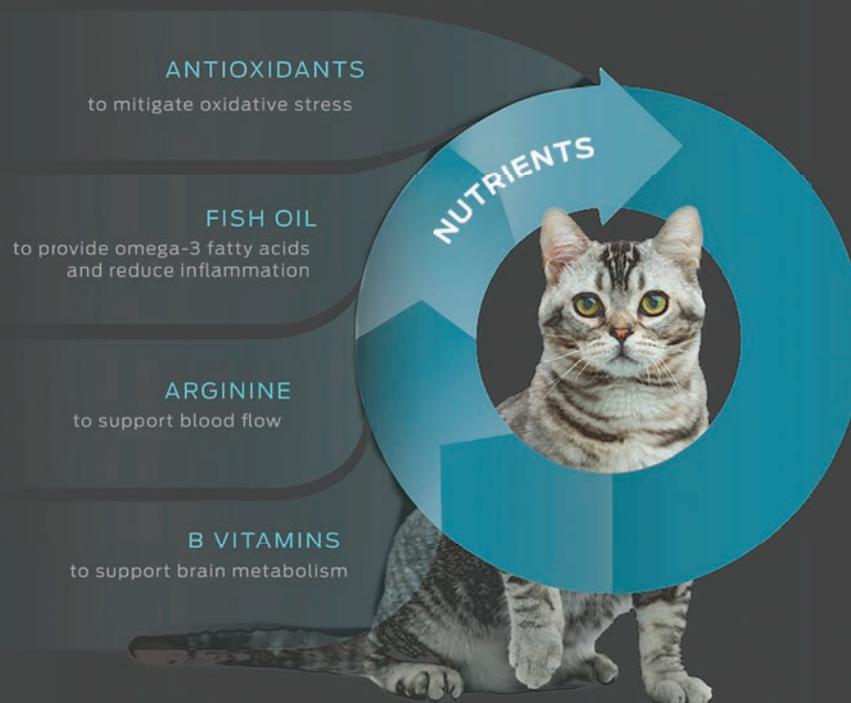
Zanghi, B. M., Gardner, C., Araujo, J., & Milgram, N. W. (2016). Diurnal changes in core body temperature, day/night locomotor activity patterns, and actigraphy-generated behavioral sleep in aged canines with varying levels of cognitive dysfunction. *Neurobiology of Sleep and Circadian Rhythms*, 1, 8-18. doi: 10.1016/j.nbscr.2016.07.001

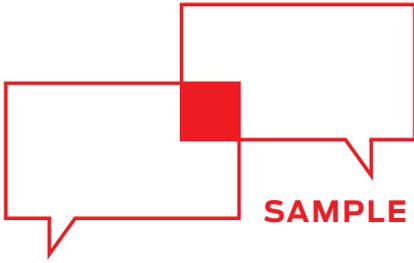
Zanghi, B. M., Araujo, J., & Milgram, N. W. (2015). Cognitive domains in the dog: independence of working memory from object learning, selective attention, and motor learning. *Animal Cognition*, 18, 789-800. doi: 10.1007/s10071-015-0847-3

ANTIOXIDANTS, OMEGA-3 FATTY ACIDS AND BRAIN PROTECTION

The developing brain has unique nutritional demands to set the foundation for lifelong brain health. Metabolic changes and risk factors associated with brain aging, age-related cognitive decline, and the resulting behavioral changes can be targeted with nutritional interventions that support healthier brain aging.

- Developing puppies need adequate dietary omega-3 fatty acids – particularly docosahexaenoic acid (DHA) – to ensure healthy brain development. *(Reynolds et al, 2006)*
- Puppies fed a diet supplemented with DHA completed a maze test over 25% faster than littermates fed a control diet, reflecting improved problem-solving ability and memory and setting the stage for a lifetime of learning. *(Reynolds et al, 2006)*
- Supplementing a senior dog's diet with a proprietary blend of antioxidants, fish oil (a primary source of omega-3 fatty acids), arginine and B vitamins improves problem-solving ability, goal-oriented behavior, and decision-making. *(Pan et al, 2018)*
- Supplementing an adult cat's diet with a proprietary blend of antioxidants, fish oil, B vitamins and arginine improves memory, learning, mental flexibility and problem solving in as little as 30 days. *(Pan et al, 2013)*





SAMPLE CONVERSATION STARTER:

“You may see a few gray hairs coming in on [his/her] muzzle, but there’s a lot more going on under the surface. By the time your pet is 6 [dogs] or 8 [cats] years old, [his/her] brain is already changing – and some of these changes are irreversible. But there are things we can do to help protect [his/her] brain through good preventive care and nutrition. By boosting [his/her] diet with targeted nutrients – such as antioxidants, fish oil, arginine and B vitamins – we can help protect brain function in [his/her] adult and senior years, and may be able to slow down or delay the onset of cognitive decline or dysfunction.”

PUBLISHED PURINA RESEARCH:

Reynolds, A. J., Waldron, M., Wilsson, E., Leavitt, Y., Dunlap, A., & Bailey, K. (2006). Effect of long-chain polyunsaturated fatty acid supplementation on mental stability, problem-solving ability, and learned pattern retention in young, growing dogs. 28. Available at https://www.researchgate.net/publication/294652556_Effect_of_long-chain_polyunsaturated_fatty_acid_supplementation_on_mental_stability_problem-solving_ability_and_learned_pattern_retention_in_young_growing_dogs.

Pan, Y., Araujo, J. A., Burrows, J., de Rivera, C., Gore, A., Bhatnagar, S., & Milgram, N. W. (2013). Cognitive enhancement in middle-aged and old cats with dietary supplementation with a nutrient blend containing fish oil, B vitamins, antioxidants and arginine. *British Journal of Nutrition*, 110, 40-49. doi: 10.1017/S0007114512004771

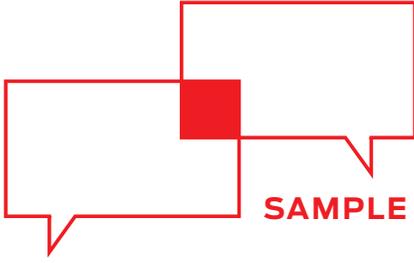
Pan, Y., Kennedy, A. D., Jönsson T. J., & Milgram, N. W. (2018). Cognitive enhancement in old dogs from dietary supplementation with a nutrient blend containing arginine, antioxidants, B vitamins and fish oil. *British Journal of Nutrition*, 119, 349-358. doi: 10.1017/S0007114517003464

COGNITIVE DECLINE AND COGNITIVE DYSFUNCTION SYNDROME (CDS)

Nutritional supplementation with medium-chain triglycerides (MCTs) provides a powerful adjunct to medical therapy through two mechanisms: providing alternative energy sources for brain cells as well as direct anti-seizure activity of MCT metabolites.

- Providing the neurons with an alternative energy source — such as ketone bodies, derived from the breakdown of MCTs — can help mitigate the glucose hypometabolism. (*Pan et al, 2010*)
- A complete and balanced diet supplemented with MCTs can improve cognitive performance in dogs with age-related cognitive decline, including promoting memory, attention and trainability in as little as 30 days. (*Pan et al, 2010*)
- Dogs with CDS, regardless of the severity, benefit from a proprietary diet containing a blend of MCT oil, omega-3 fatty acids, B vitamins, antioxidants and arginine. Signs of improvement may be observed within the first 30 days of feeding, with even more improvement noticed by 90 days. (*Pan et al, 2018*)
- Feeding CDS-affected dogs the proprietary MCT blend leads to significant improvement in 5 of 6 DISHAA categories of CDS-associated behaviors within 30 days, and in all 6 within 90 days. (*Pan et al, 2018*)

D DISORIENTATION	<ul style="list-style-type: none">• Gets stuck, difficulty getting around objects, goes to hinge side of door• Stares blankly at walls, floor, or into space• Does not recognize familiar people/familiar pets• Gets lost in home or yard• Less reactive to visual (sights) or auditory (sounds) stimuli
I SOCIAL INTERACTIONS	<ul style="list-style-type: none">• More irritable/fearful/aggressive with visitors, family or other animals• Decreased interest in approaching, greeting or affection/petting
S SLEEP/WAKE CYCLES	<ul style="list-style-type: none">• Pacing/restless/sleeps less/waking at night• Vocalization at night
H HOUSESOILING, LEARNING AND MEMORY	<ul style="list-style-type: none">• Less able to learn new tasks or respond to previously learned commands/name/work• Indoor soiling of urine or stool/decreased signaling to go out• Difficulty getting dog's attention/increased distraction/decreased focus
A ACTIVITY	<ul style="list-style-type: none">• Decrease in exploration or play with toys, family members, other pets• Increased activity, including aimless pacing or wandering• Repetitive behaviors (e.g., circling/chewing/licking/stargazing)
A ANXIETY	<ul style="list-style-type: none">• Increased anxiety when separated from owners• More reactive/fearful to visual (sights) or auditory (sounds) stimuli• Increased fear of places/locations (e.g., new environments/going outdoors)



SAMPLE CONVERSATION STARTER:

“Although some changes in cognition can be expected with aging, accelerated changes in the brain lead to behaviors associated with what is called cognitive dysfunction syndrome – such as wandering at night, changes in social interactions with family members, and appearing confused or disoriented. These aren’t signs of normal aging, and it’s critical that we take action now to protect brain function and try to slow down the process so you and your dog can enjoy [his/her] senior years as much as possible. One way we can do this is by feeding a diet that includes medium-chain triglycerides (MCTs) and other nutrients that support brain function. Studies have shown improvement in senior dogs’ cognition and behaviors with this approach.”

PUBLISHED PURINA RESEARCH:

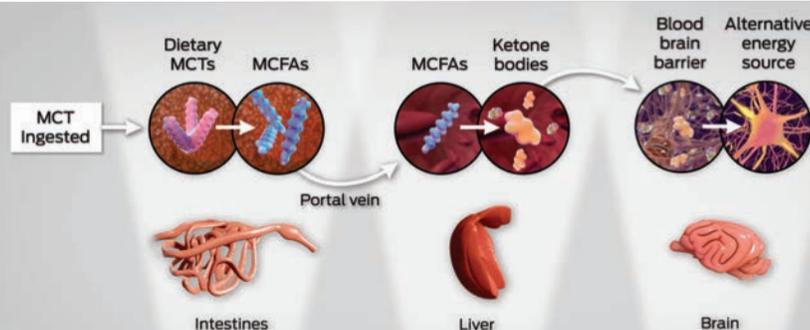
Pan, Y., Larson, B., Araujo, J. A., Lau, W., de Rivera, C., Santana, R., Gore, A., & Milgram, N. W. (2010). Dietary supplementation with medium-chain TAG has long-lasting cognition-enhancing effects in aged dogs. *British Journal of Nutrition*, 103, 1746-1754. doi: 10.1017/S0007114510000097

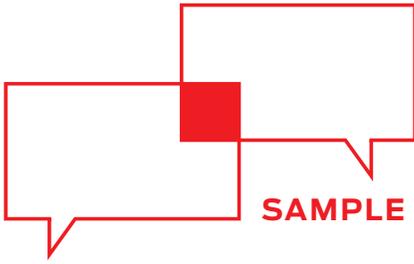
Pan, Y., Landsberg, G., Mougeot, I., Kelly, S., Xu, H., Bhatnagar, S., Gardner, C. L., & Milgram, N. W. (2018). Efficacy of a therapeutic diet on dogs with signs of cognitive dysfunction syndrome (CDS): A prospective double blinded placebo controlled clinical study. *Frontiers in Nutrition*, 5, article 127. doi: 10.3389/fnut.2018.00127

MEDIUM-CHAIN TRIGLYCERIDES FOR IDIOPATHIC EPILEPSY AND ASSOCIATED BEHAVIORS IN DOGS

Nutritional supplementation with medium-chain triglycerides (MCTs) provides a powerful adjunct to medical therapy through two mechanisms: providing alternative energy sources for brain cells as well as direct anti-seizure activity of MCT metabolites.

- More than two-thirds (71%) of dogs with refractory idiopathic epilepsy showed an overall reduction in seizure frequency when fed a complete and balanced diet supplemented with MCTs, with almost half of those dogs showing a 50% or greater reduction in seizure frequency and 1 in 7 dogs becoming seizure-free. (*Law et al, 2015*)
- More than three-quarters (81%) of dogs with refractory idiopathic epilepsy showed a reduction in the number of seizure days (the number of days in a month with seizures) when fed a diet supplemented with MCTs. (*Law et al, 2015*)
- The effects of the MCT-supplemented diet were seen as early as the first day for some dogs. (*Law et al, 2015*)
- The MCT-supplemented diet did not significantly affect the plasma concentrations of phenobarbital or potassium bromide. (*Law et al, 2015*)
- In conjunction with anti-epileptic drugs, dietary supplementation with MCTs can reduce seizure frequency in dogs with idiopathic epilepsy. (*Law et al, 2015*)
- Nutrition may serve as a valuable adjunct to traditional medical therapy in the management of dogs with this chronic neurological condition.
- Dogs with idiopathic epilepsy can also exhibit ADHD-like behaviors – predominantly high excitability and chasing behavior, resulting in low trainability scores. (*Packer et al, 2016*)
- Feeding epileptic dogs a complete and balanced diet with 5.5% MCT oil reduced two ADHD-like behaviors (chasing behavior and stranger-related fear). (*Packer et al, 2016*)
- Dogs with idiopathic epilepsy are more likely to develop cognitive dysfunction syndrome (CDS) at a younger age. (*Packer et al, 2018*)





SAMPLE CONVERSATION STARTERS:

“Your dog has been diagnosed with idiopathic epilepsy, and will require regular medication to try to keep [his/her] seizures under control. I also recommend that we change [his/her] diet, because a combination of medications and nutrition has been shown to help reduce seizures. Studies have shown that adding medium-chain triglycerides to an epileptic dog’s diet reduces seizures as well as some of the ADHD-like behaviors that may also be seen with epilepsy.”

OR

“Your dog’s epilepsy isn’t as controlled with medications as I’d like to see it, so I’m recommending that we make a change to [his/her] diet because a combination of nutrition and anti-epilepsy medications may work better for reducing seizures than the medications alone.”

OR

“Your dog is showing some of the behavioral changes that are often associated with epilepsy. I’d like to make a change to [his/her] diet to include medium-chain triglycerides and other nutrients that have been shown to improve some of these behaviors as well as reduce seizures in epileptic dogs.”

PUBLISHED PURINA RESEARCH:

Law, T. H., Davies, E. S., Pan, Y., Zanghi, B., Want, E., & Volk, H. A. (2015). A randomised trial of a medium-chain TAG diet as treatment for dogs with idiopathic epilepsy. *British Journal of Nutrition*, 114, 1438–1447. doi: 10.1017/S000711451500313X Erratum in: *British Journal of Nutrition*, (2016); 115:1696.

Packer, R. M. A., Law, T. H., Davies, E., Zanghi, B. M., Pan, Y., & Volk, H. A. (2016). Effects of a ketogenic diet on ADHD-like behavior in dogs with idiopathic epilepsy. *Epilepsy & Behavior*, 55, 62-68. doi: 10.1016/j.yebeh.2015.11.014

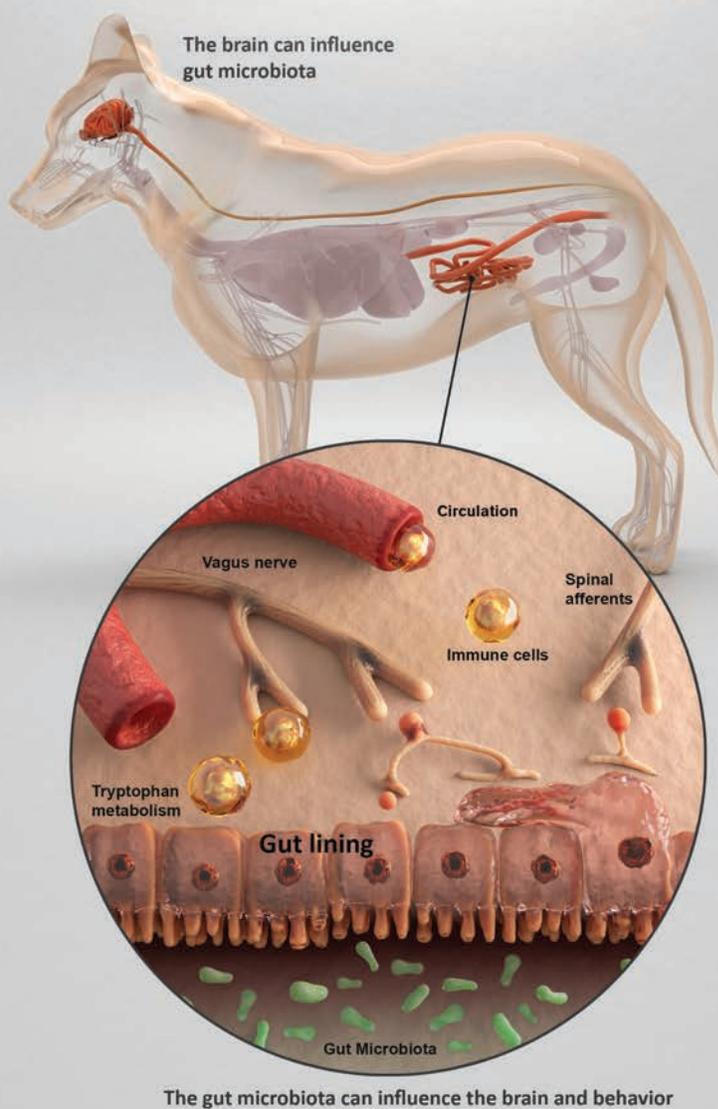
OTHER REFERENCES:

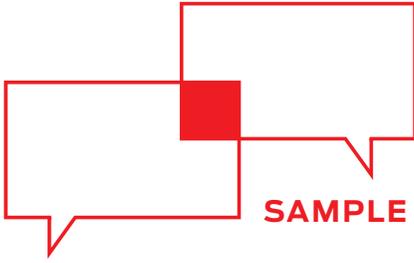
Packer, R. M. A., McGreevy, P. D., Salvin, H. E., Valenzuela, M. J., Chaplin, C. M., & Volk, H. A. (2018). Cognitive dysfunction in naturally occurring canine idiopathic epilepsy. *PLOS One*, 13, e0192812. doi: 10.1371/journal.pone.0192182

ADDRESSING BRAIN HEALTH THROUGH THE GUT AND MICROBIOME

The brain maintains bidirectional communication with the gut (via the gut-brain axis) which is mediated, in part, by the gut microbiota. Altering the gut microbiota through nutritional interventions has the potential to facilitate cross talk between the brain and gut, and to influence behavior. As researchers continue to discover links between dysbiosis and health conditions such as cognitive changes and anxiety, new roles for nutrition in brain health will emerge.

- In a blinded crossover study, anxious behaviors improved in 90% of anxious dogs supplemented with a specific strain of *Bifidobacterium longum*. (McGowan, 2016)





SAMPLE CONVERSATION STARTER:

“Anxiety in dogs is real. There are medications available, and positive reinforcement training can help manage [his/her] anxious reactions to some triggers. There is also growing scientific evidence that the gut has more impact on brain health and behavior than we’ve previously thought. There’s evidence in people and in dogs that diet-induced changes in the gut can trigger changes in a number of behaviors, including anxiety.”

PUBLISHED PURINA RESEARCH:

McGowan, R. T. S. (2016). Oiling the brain or Cultivating the gut: Impact of diet on anxious behaviors in dogs. Proceedings of the Nestlé Purina Companion Animal Nutrition Summit, March 31-April, Florida, 91-97.