Effect of dietary protein content and tryptophan supplementation on dominance aggression, territorial aggression, and hyperactivity in dogs

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Objective—To evaluate the effect of high- and low-protein diets with or without tryptophan supplementation on behavior of dogs with dominance aggression, territorial aggression, and hyperactivity.

Design—Prospective crossover study.

Animals—11 dogs with dominance aggression, 11 dogs with territorial aggression, and 11 dogs with hyperactivity.

Procedure—In each group, 4 diets were fed for 1 week each in random order with a transition period of not < 3 days between each diet. Two diets had low protein content (approximately 18%), and 2 diets had high protein content (approximately 30%). Two of the diets (1 low-protein and 1 high-protein) were supplemented with tryptophan. Owners scored their dog's behavior daily by use of customized behavioral score sheets. Mean weekly values of 5 behavioral measures and serum concentrations of serotonin and tryptophan were determined at the end of each dietary period.

Results—For dominance aggression, behavioral scores were highest in dogs fed unsupplemented high-protein rations. Tryptophan-supplemented low-protein diets were associated with significantly lower behavioral scores than low-protein diets without tryptophan supplements.

Conclusions and Clinical Relevance—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. (*J Am Vet Med Assoc* 2000;217:504–508)

The effect of food composition on the behavior of mammals has been appreciated for many years.[1,2] In dogs, the link between dietary protein content, metabolism of the amino acid tryptophan, and aggressive behavior has been the subject of considerable interest and discussion.[3] Dogs fed a **low-protein (LP)** diet had decreased territorial aggression in a previous study.[3] Low-protein diets, in conjunction with high carbohydrate content, may induce their effect by changing the plasma ratio of the amino acid **L-tryptophan (Trp)** to other **large neutral amino acids (LNAA)**, thus affecting competition between Trp and LNAA for a common blood-brain barrier transporter mechanism.[4,5] Most proteins are low in Trp and rich in LNAA so that feeding a **high-protein (HP)** diet will reduce the Trp:LNAA, impairing the transfer of Trp across the blood-brain barrier.[6] Conversely, LP diets result in higher Trp:LNAA, thus enhancing Trp transfer to the brain.[7] Because Trp is a biosynthetic precursor for the neurotransmitter serotonin,[8] decreased concentration of this amino acid will lead to reduced formation of serotonin and possibly more aggressive responses to stimuli.[6,9,10] As corroboratory evidence of this hypothesis, results of studies in humans indicate that diets low in Trp increase aggression, anger, and depression,[11,12] whereas increased dietary Trp has a therapeutic effect in pathologically aggressive patients[13] and promotes a feeling of well-being in people with aggressive traits.[12] In support of the hypothesis regarding serotonin and aggression, dogs that are dominant and aggressive have lower mean CSF concentration of the serotonin metabolite **5-Hydroxyindoleaceticacid (5-HIAA)** than nonaggressive control dogs.[14]

The purpose of the study reported here was to evaluate the effect of HP and LP diets with or without Trp supplementation on behavior of dogs with dominance aggression, territorial aggression, and hyperactivity. We hypothesized that LP diets and diets high in Trp would be associated with less aggression and reduced excitability and reactivity.

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Materials and Methods

Study enrollment—Thirty-eight client-owned dogs of various ages, breeds, and sexes were serially enrolled in the study; 33 dogs completed the study, whereas 5 dogs did not complete the study for various reasons. All dogs were patients at Tufts University Veterinary School Behavior Clinic and the study protocol was approved by the Tufts Animal Care and Use Committee. Each dog was required to meet specific behavioral criteria for dominance aggression, hyperactivity, or territorial aggression (**Appendices 1-3**) and their owners were required to agree to the terms and conditions of the study and sign a consent form. Dogs were not enrolled if they were pregnant, < 5 months of age, had received psychoactive medication within 2 weeks of initiation of the study, had a physical status score of < 3 (on a 1-to-5 scale)[15] or, because of their aggressive behavior, were an immediate danger to people. A full medical history, physical examination, CBC, and serum biochemical analyses were performed to screen for diseases other than behavioral abnormalities.

Study design—Dogs meeting study criteria were

Table 1—Composition of experimental diets that contained low (LP) or high (HP) concentrations of proteins and were supplemented with L-tryptophan (+Trp) or were not supplemented (−Trp)

Ingredient	LP−Trp	LP+Trp	HP−Trp	HP+Trp
Corn	370	370	200	200
Poultry meal	184	184	410	410
Corn starch	156.5	155.05	295.5	294.05
Animal fat	100	100	20	20
Dried eggs	32.5	32.5	32.5	32.5
Cellulose	100	100	0	0
Natural flavor[a]	20	20	20	20
Dicalcium phosphate	15	15	0	0
Vegetable oil	10	10	10	10
Minerals[b]	9.4	9.4	9.4	9.4
Vitamins[c]	2.5	2.5	2.5	2.5
Ethoxyquin	0.1	0.1	0.1	0.1
L-Tryptophan	0	1.45	0	1.45

Values are reported as g/kg. To convert to g/lb, divide by 2.2.
[a]Liquid palatability enhancer. [b]Potassium chloride, sodium chloride, ferrous sulfate, zinc oxide, copper sulfate, manganous oxide, calcium iodate, cobalt carbonate, and sodium selenite. Mineral concentrations met or exceeded established standards. [c]Choline chloride, vitamin A, vitamin D3, vitamin E, niacin, calcium pantothenate, thiamin mononitrate, riboflavin, pyridoxine hydrochloride, folic acid, biotin, and vitamin B_{12}. Vitamin concentrations met or exceeded established standards.

Table 2—Nutrient analysis of experimental diets that contained low or high concentrations of proteins and were supplemented with L-tryptophan or were not supplemented

Nutrients	LP−Trp	LP+Trp	HP−Trp	HP+Trp
Protein	186	188	308	315
Fat	171	175	122	111
Crude fiber	82	73	16	14
Ash	50	50	53	54
Metabolizable energy (kcal/kg)	3715	3789	3554	3490
Amino acids				
Tryptophan	1.8	3.0	2.4	3.7
Arginine	10	10	18	18
Histidine	5	5	7	7
Isoleucine	7	7	12	12
Leucine	15	15	23	23
Lysine	9	9	14	14
Methionine	3	3	4	4
Phenylalanine	7	7	12	12
Tyrosine	3.1	3.2	5.9	6.1
Threonine	7	7	12	12
Valine	9	9	16	16
Trp:LNAA	0.04:1	0.07:1	0.04:1	0.06:1

Values are expressed as g/kg unless indicated otherwise.
LNAA = Large neutral amino acids.

enrolled into 1 of 3 study groups, including a dominance aggression group, a territorial aggression group, and a hyperactivity group. For each group, 4 diets were fed for a 1-week period each, in random order, with a transitional period of at least 3 days between each diet. Minimum total duration of the study for each dog was 40 days. A LP diet without supplemental Trp was designated LP–Trp, whereas a LP diet with supplemental Trp was designated LP+Trp **(Table 1 and 2)**. A HP diet without supplemental Trp was designated HP–Trp, whereas a HP diet with supplemental Trp was designated HP+Trp. Because of supplementation, the Trp:LNAA was higher in the supplemented diets, compared with the unsupplemented diets (LNAA concentration in the diets was not determined). Diets met standards of the Association of American Feed Control Officials Nutrient Profiles for Adult Dogs and were fed to provide a daily metabolizable energy intake of 1.6 × (70 kcal × body weight [kg]$^{0.75}$). Thus, for a dog that weighed 10 kg (22 lb), approximate daily Trp intake was 30, 50, 42, and 67 mg/d for LP–Trp, LP+Trp, HP–Trp, and HP+Trp diets, respectively. Diets were coded numerically and by a color code. Content of each diet was unknown to the clinicians involved in the study. Owners were instructed to feed the study diet exclusively and offer each dog 2 meals/d; amount fed was determined on the basis of each dog's body weight. By use of the behavioral scores (Appendices 1-3), owners scored their dogs daily for dominance aggression, territorial aggression, fearfulness, hyperactivity, and excitability.

Serotonin and Trp analyses—For measurement of serum Trp and serotonin concentrations, venous blood samples were obtained at the end of each week of the trial while each dog was still receiving a test diet. Sampling was conducted 1 to 2 hours after a meal to minimize the effect of postprandial variations in concentration of Trp and serotonin. Blood was drawn into a polyethylene syringe and transferred to a tube containing EDTA as anticoagulant. Samples were centrifuged for 10 minutes at 500 × g, and plasma was removed, frozen immediately, and stored at –80 C (–112 F) for up to 2 months until time of analysis. For analysis, samples were thawed and proteins were removed by centrifugation for 5 minutes at 9,000 × g after addition of an internal standard (100 µl of $10^{-6}M$ N-methylserotonin) and 100 µl of 0.5*M* perchloric acid to 0.5 ml of plasma. Aliquots of the supernatant were injected into a high-performance liquid chromatography apparatus equipped with either a 5-µm carbon 18 reversed-phase column[a] and a coulometric detector[b] or a 2-µm carbon 18 reversed-phase column[c] and an amperometric detector.[16,17,d] Concentrations of serotonin and Trp were calculated from peak heights, relative to an internal standard. Peak heights were adjusted relative to the internal standard and compared with a standard curve generated on the same day. To permit a direct comparison, serotonin and Trp were calculated in molar amounts. All assays were carried out in duplicate, and standard curves were run each day.

Statistical analyses—Mean values were determined for results of 5 behavioral measurements that were recorded daily by owners during each of the dietary periods. Visual examination of the behavior data revealed that assumption of normal distributions was appropriate. Because results of Trp and serotonin analyses were not normally distributed, these data were logarithmically transformed before analysis. Each variable was analyzed independently, by use of ANOVA to first test the effects of order of fed diets and then to test significance of the 2 dietary factors (protein concentration, effect of Trp supplementation) nested within experimental groups. Interaction terms were included in the initial method and removed if not significant. The least-significant differences method was used for post hoc analysis of differences between behavior groups. All analyses were performed with computer software.[e] Differences were considered significant at $P < 0.05$.

Results

Eleven dogs in each group completed the study; mean ± SD age of territorial aggressive dogs was 3.7 ± 1.7 years (range, 1.5 to 8.5 years), mean age of dominant aggressive dogs was 5.4 ± 3.7 years (range, 2.5 to 14 years), and mean age of hyperactive dogs was 3.6 ± 2.2 years (range, 1.9 to 9.1 years).

Behavior—Significant changes in behavior were not detected within any of the 3 groups for any of the dietary treatments. As expected, dogs in the dominance aggression group had significantly higher dominance scores ($P = 0.002$) than dogs in the other 2 groups. After correcting for this factor, each behavior was examined across behavioral groups for the entire study population as a whole. By use of this

Table 3—Mean (± SE) daily behavioral scores (corrected for group differences) for 33 dogs fed diets that contained low or high concentrations of proteins and were supplemented with L-tryptophan or were not supplemented

Behavior	LP−Trp	LP+Trp	HP−Trp	HP+Trp
Dominance aggression	1.12 ± 0.17	1.29 ± 0.17	1.84 ± 0.17[a]	1.04 ± 0.18
Territoriality	3.68 ± 0.15[b]	3.17 ± 0.15	3.47 ± 0.15	3.33 ± 0.16
Fear	2.34 ± 0.15	2.40 ± 0.15	2.29 ± 0.15	2.25 ± 0.15
Hyperactivity	3.58 ± 0.10	3.46 ± 0.10	3.46 ± 0.10	3.40 ± 0.10
Excitability	3.7 ± 0.11	3.5 ± 0.11	3.66 ± 0.11	3.53 ± 0.11

[a]HP−Trp versus HP+Trp, $P = 0.001$; HP−Trp versus LP+Trp, $P = 0.024$; HP−Trp versus LP−Trp, $P = 0.003$. [b]LP+Trp versus LP−Trp, $P = 0.022$.

analysis, significant differences were detected between diet groups for certain behaviors (**Table 3**). Dominance scores for dogs fed the HP-Trp diet were significantly higher than those of dogs fed the other 3 diets.

Territoriality scores among dogs in the different behavioral groups were not significantly different. Territoriality scores were significantly higher for dogs fed the LP–Trp diet, compared with those fed the LP+Trp diet.

Significant differences in fearfulness were not detected among the 3 behavioral groups or in all dogs among the 4 diets. Hyperactivity and excitability responses differed ($P < 0.001$) among the behavioral groups; hyperactive dogs had the highest scores, dominant aggressive dogs had intermediate scores, and territorial aggressive dogs had the lowest scores. After correcting for these differences and analyzing data from all dogs, significant differences for hyperactivity and excitability scores were not detected among the 4 diets.

Plasma Trp and serotonin concentrations— Significant differences were not detected among behavioral groups or diets for plasma tryptophan or serotonin concentrations. The natural log of the plasma tryptophan concentration (nmol/ml) for the various diets were as follows (mean ± SE): LP–Trp, 2.49 ± 0.13, LP + Trp, 2.53 ± 0.12; HP–Trp, 2.78 ± 0.12; HP+Trp, 2.66 ± 0.12; all diets (mean ± SD), 2.61 ± 0.69. The natural log of the plasma serotonin concentration (pmol/ml) for the various diets were as follows: LP–Trp, 2.78 ± 0.18; LP+Trp, 2.59 ± 0.19; HP–Trp 2.79, ± 0.19; HP+Trp, 2.72 ± 0.18; and all diets (mean ± SD) 2.70 ± 0.90.

Discussion

As a whole, results of our study supported the hypothesis being tested. The finding that Trp supplementation of the HP and LP diets of dogs with dominance and territorial aggression, respectively, induced a significant decrease in aggression scores was anticipated. Both of these Trp-supplemented diets had higher Trp:LNAA than the 2 unsupplemented diets; the higher ratio may have resulted in a greater proportion of Trp crossing the blood-brain barrier, increasing brain serotonin concentration and decreasing aggression. A factor that may have been operating with regard to the HP diets is that increased dietary protein concentration increases plasma concentrations of tyrosine and phenylalanine,[18] which are both catecholamine precursors; this change could effectively reduce the threshold for aggression.[19,20] Addition of Trp (as in the HP+Trp diet) should counter this effect by increasing brain serotonin concentration, thus reducing aggression. Increasing brain serotonin concentration usually decreases aggression[21,f]; however, the direction of modulation of behavior induced by serotonin varies according to the animal's social status.[22] Furthermore, the behavior-modifying effect induced by altering Trp concentration depends critically on circumstance.[23] Dominant animals, unlike their subordinate counterparts, may have high, possibly fluctuating, concentrations of brain serotonin,[24] making stabilization of regional brain serotonin, rather than absolute changes in its concentration, more important in terms of minimizing aggression.

Another important finding was that addition of Trp to a LP diet reduced territoriality scores. The LP+Trp diet had a higher Trp:LNAA that presumably resulted in increased serotonin synthesis.[25] Results of an earlier study indicate that LP diets are associated with a reduction in territorial-fear aggression in dogs.[3] This finding was not replicated in our study. Territoriality scores for dogs fed the LP+Trp diet were lower than those of dogs fed either of the HP diets, but differences were not significant.

The lack of influence of dietary protein content or addition of Trp to the diet on the behavior of hyperactive dogs was not unexpected, because results of recent studies[23,26,27] indicate no improvement in behavior of hyperactive laboratory animals and children treated with selective serotonin reuptake inhibitors. If potent serotonin-enhancing strategies, like the use of selective serotonin reuptake inhibitors, are ineffective in changing hyperactive behavior, it is unlikely that more subtle measures such as dietary changes would induce an observable effect.

Plasma concentrations of serotonin and Trp were surprisingly consistent in all phases of our study, despite different concentrations of dietary Trp. We had expected that dietary differences would cause measurable change in the plasma concentrations of these substrates; lack of such changes could indicate that the analytic method we used was inadequate. Alternatively, we may have missed peak plasma concentrations of these substrates by obtaining samples 1 to 2 hours after a meal; recent evidence indicates that peak changes in Trp concentration may not develop until 5 hours after a meal is fed.[9] Correlation between plasma serotonin and Trp concentrations was expected, because these are dependent variables. It may be more meaningful to measure platelet serotonin concentration.

Results of the study reported here have potential applications for treatment of behavioral problems in dogs. Low-protein or Trp-rich diets may be helpful adjuncts in the management of dominance aggression. Also, LP diets supplemented with Trp may be beneficial in reducing territorial aggression in dogs. One caveat regarding LP diets, however, is that they should be used only under strict nutritional guidance in young, growing dogs (< 6 months of age) and in pregnant and lactating bitches.

Appendix 1

Behavioral criteria for enrollment and assessment of dominant aggressive dogs

1) Diagnosis of dominance aggression made by a behaviorist on the basis of history and clinical findings.
2) Dogs reacted aggressively to family members in ≥ 5 of 30 dominance aggression promoting situations[3] and had some aggressive behavior at least 5 d/wk.
3) Daily dominance score ranged from 0 to 10. Criterion for a score of 1: single episode of mild aggression (growls, lifts lip, or threatens). Criterion for a score of 2: several episodes of mild aggression. Criterion for a score of 3: mild aggression in many circumstances. Criterion for a score of 4: single episode of snapping. Criterion for a score of 5: several episodes of snapping. Criterion for a score of 6: snaps in many circumstances (bites without breaking skin). Criterion for a score of 7: bites without breaking skin in several circumstances. Criterion for a score of 8: bites once (bruising or breaking skin). Criteria for a score of 9: bites in several circumstances (breaking skin or bruising, lunges, or chases repeatedly), but dog can be controlled with discipline. Criteria for a score of 10: bites (breaking skin or bruising), lunges, or chases repeatedly in many circumstances; discipline escalates the aggression.

Appendix 2

Behavioral criteria for enrollment and assessment of hyperactive dogs

1) Diagnosis of hyperactivity made by a behaviorist on the basis of history and clinical findings.
2) Mean daily score ≥ 5 for either a hyperactivity daily assessment scale or an excitability scale. The hyperactivity scale (range, 0 to 10) was based on the number of hyperactive actions that were performed during each day. The 10 hyperactive actions were excessive pacing or circling, not remaining in sit-stay or down-stay positions when required, excessive chewing of objects or self-mutilation, being easily distracted by extraneous stimuli, impulsive behavior (not waiting), not engaging in any particular activity for an extended period (limited attention span), playing roughly, barking or whining excessively, acting in an intrusive manner, and not heeding commands. The excitability scale (range, 0 to 10) was based on assessment of the dog in 4 situations; mean values of scores recorded during the 4 situations were used. The first situation involved the dog's behavior at home during the daytime; a score of 0 was assigned if the dog spent most of this period asleep, whereas a score of 10 was assigned if the dog paced and panted continuously; scores from 1 to 9 were assigned on the basis of owner's subjective assessment of the dog's behavior between these extremes. The second situation was the dog's reaction to the doorbell or outside noise; a score of 0 was assigned if the dog had no reaction, whereas a score of 10 was assigned if the dog reacted with uncontrollable excitement; scores from 1 to 9 were assigned on the basis of owner's subjective assessment of the dog's behavior between these extremes. The third situation involved the dog's behavior during walks; a score of 0 was assigned if the dog lagged behind the owner, whereas a score of 10 was assigned if the dog was uncontrollable; scores from 1 to 9 were assigned on the basis of owner's subjective assessment of the dog's behavior between these extremes. The fourth situation involved the time required for the dog to resume calm behavior after stimulation; a score of 0 was assigned if the dog became calm immediately, whereas a score of 10 was assigned if the dog remained excited indefinitely; scores from 1to 9 were assigned on the basis of owner's subjective assessment of the dog's behavior between these extremes.
3) Hyperactive dogs also had to have dominance score ≤ 2.

Appendix 3

Behavioral criteria for enrollment and assessment of territorial aggressive dogs

1) Diagnosis of territorial aggression was made by a behaviorist on the basis of history and clinical findings.
2) Mean daily territorial aggression score ≥ 5. The territorial aggression scale ranged from 0 to 10; a score of 0 was assigned if the dog did not bark or make menacing postures or motions when strangers approached or enter the house, whereas a score of 10 was assigned if the dog was uncontrollably aggressive when a stranger approached the house (barking, growling, baring teeth, charging the door, and similar behaviors); scores from 1 to 9 were assigned on the basis of owner's subjective assessment of the dog's behavior between these extremes.
3) Mean daily fearfulness score ≥ 3. The fearfulness scale ranged from 0 to 10; a score of 0 was assigned if the dog appeared relaxed and happy under all circumstances, without signs of fearfulness at any time, whereas a score of 10 was assigned if the dog had signs of extreme fear when confronted by any strange person, situation, or experience, or if the dog constantly followed the owner from room to room and could not be left alone without risk of damaging itself or property.
4) Territorial aggressive dogs also had to have dominance score ≤ 2 and hyperactive score ≤ 2.

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Correction: Effect of timing of blood collection on serum phenobarbital concentrations in dogs with epilepsy

In the Results and Discussion sections of "Effect of timing of blood collection on serum phenobarbital concentrations in dogs with epilepsy" (*JAVMA*, 2000; 217:200-204), the dosages were converted from mg/kg to mg/lb incorrectly.

All mg/kg dosages are stated correctly; these values should then be divided by 2.2 when converting to mg/lb. For example, in the first paragraph of the Results section, it states, "Dosages of phenobarbital ranged from 1.0 mg/kg/d [2.2 mg/lb/d] to 10.9 mg/kg/d [24 mg/lb/d]"; this should read, "…1.0 mg/kg/d [0.45 mg/lb/d] to 10.9 mg/kg/d [4.9 mg/lb/d]."