



Integrating the gut-brain axis, CBD, and melatonin in the management of anxiety and frustration-driven displacement behavior in a Lagotto Romagnolo: An integrated approach

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Abstract: Ettore, a two-and-a-half-year-old male Lagotto Romagnolo, underwent a behavioral visit due to difficulty staying calm at home in the presence of the female caregiver. The manifested symptoms—hyperactivity, constant demands for interaction, and displacement behaviors (e.g., scratching, pacing, destructiveness)—were interpreted as the expression of an underlying anxiety exacerbated by chronic frustration, typical of high-drive dogs. The onset coincided with a modification in the female caregiver schedule and diminished availability. The therapeutic protocol integrated melatonin and cannabidiol (CBD) for their anxiolytic and wellness-enhancing effects, alongside focused support for the gut-brain axis, together with a targeted behavioral and environmental modification intervention. Subsequent follow-ups showed a significant decrease in restlessness and an enhancement in autonomy, validating the effectiveness of a multimodal management strategy that incorporates medication, emotional support, and a focus on gut health.

Key Words: anxiety disorder; microbiota; nutraceutical; working dog, combined approach.

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Introduction

Anxiety and hyperactivity within the domestic setting constitute a prevalent issue in veterinary behavioral medicine, especially in breeds chosen for their elevated work drive and physical activity, such as the Lagotto Romagnolo. In these individuals, an insufficient or deteriorating routine may induce persistent frustration, which might further aggravate an underlying anxiety condition (Casey et al., 2022). The observed clinical indications, including displacement behaviors (shaving, turning) and hyperactivity, frequently stem from psychological stress and the dog's coping mechanisms. To tackle this intricate issue, behavioral medicine increasingly employs multimodal strategies that combine behavioral therapy with nutraceutical and pharmaceutical support (Niyyat et al., 2018; d'Angelo et al., 2022; Scandurra et al., 2022; Sacchettino et al., 2023b; Giuliano et al., 2024). Indeed, cannabidiol (CBD) and melatonin are experiencing significant success in veterinary medicine for stress control. CBD has garnered attention for potential anxiolytic and anxiolytic effects, modulating the hypothalamic-pituitary-adrenal (HPA) axis while fostering an overall sense of well-being (Di Salvo et al., 2023; Flint et al., 2024; Opyd, 2025). In veterinary clinical practice, melatonin is widely utilized off-label to address emotional discomfort, owing to its advantageous safety profile and convenience of administration, diminishing preoperative alertness and anxiety (Niggemann et al., 2019) while additionally lowering cortisol levels in response to physiological stress (Salavati et al., 2023; Song&Yoon,2025). Furthermore, scientific interest in the gut-brain axis and behavior modulation is increasing, as recent data associate altered microbial profiles (i.e., dysbiosis) with anxiety and fear (Sacchettino et al., 2025, Sacoor et al., 2024). Bidirectional interactions along this axis are known to significantly influence canine anxiety disorders, presenting new challenges for veterinary medicine in using psychobiotics to regulate emotional dominance (Sacoor et al., 2024). The purpose of this clinical case study is

to describe the response to the one-year integrated treatment given to a Lagotto Romagnolo who was diagnosed with an anxiety disorder and chronic frustration.

Case Presentation

Ettore is a two-and-a-half-year-old intact male Lagotto Romagnolo. He was adopted, at two months from a working-line breeder. At present, he resides with a couple in a suburban setting, near a forest. The caregivers requested a behavioral examination since Ettore struggles to remain calm in a home setting and consistently seeks interaction when the female caregiver is present. His routine was primarily focused on fulfilling his high breed drive, in line with the high working drive suggested by the breeder, incorporating long daily walks with his caregivers (some reaching up to 15 km) and including a significant element of performative activities and olfactory research. During walks, Ettore is quite exploratory and engages his sense of smell intensely. The routine also featured caregivers-managed morning chewing sessions, which included food toys, rabbit ears, and pig ears. He often vomited after consuming food too quickly. The caregivers observed that while Ettore stays calm during the chewing activity, he quickly transitions into a state of constant exploration once it concludes. In addition, Ettore had suffered multiple episodes of gastroenteritis, which were treated with antibiotics, and there has been a recent adjustment in his diet. The behavioral history linked the onset of symptoms to a decrease in the time the female caregiver spent with the dog after starting a new job, disrupting the previous routine's balance. Clinical signs observed in the home included hyperactivity, scratching (at surfaces), digging, spinning, and attention-seeking requests, which were often manifested through destructive acts (such as damaging the couch cover) predominantly performed in the female caregiver's presence. The caregivers reported no issues with sleep, except when they rose during the night to use the bathroom. In such instances, Ettore ensured they safely reached the bathroom before returning to sleep, demonstrating a keen sense of social vigilance.

Diagnostic Evaluation and Treatment

Diagnostic hypothesis

The diagnostic hypothesis was anxiety disorder (intermittent anxious state) (Masson et al., 2024), with situational anxiety and phobia being ruled out (Gazzano & Ogi, 2020; Landsberg et al., 2023). The clinical signs were severely amplified by frustration (Casey et al., 2022; Landsberg et al., 2013) related to his high working drive and reduced social interaction, resulting in secondary reinforcement-maintained attention-seeking behaviors.

Treatment

At the end of the behavioral visit, it was prescribed to administer melatonin (2 tablets twice daily) plus CBD 10% full spectrum (2 drop in the morning and 2 in the evening) plus psychobiotics based on *Lactobacillus rhamnosus*, *Lactobacillus acidophilus*, and *Lactobacillus reuteri* (Psico-brain®, 1 tablet in the evening). Initial dosages were calculated based on the dog's body weight and adjusted during follow-up, in line with the "Start low and go slow" approach (MacCallum & Russo, 2018). Behavioral prescriptions were provided to enhance calm environments and diminish stimulating activities, particularly those associated with search tasks in wooded areas.

Follow-up

Followed up in 30 days after initiating therapy, the caregivers reported that Ettore was significantly more relaxed; they observed many more instances of calmness and independence. Addi-

tionally, they monitored hematobiochemical parameters, all of which were within normal limits. It was agreed upon to continue with the same plan of treatment for an additional month, warning caregivers that relapses could occur because of the Christmas holiday. Followed up in two months, the caregivers reported that Ettore had experienced a period of decline due to changes in holiday habits during Christmas, compounded by the time spent apart from his female caregiver at home due to COVID-19. Nevertheless, at the time of follow-up, the caregivers reported that the condition had shown considerable improvement since the holidays. He experienced brief periods of evening restlessness, during which he tended to chew his bed. Therefore, it was essential to promote the practice of evening chewing (Uccheddu et al., 2024) by incorporating a Kong stuffed with moist gastrointestinal food. It was also recommended to substitute Psicobrain® with the probiotic Enterelle® (*Saccharomyces cerevisiae* sub. *boulardii*, *Lactobacillus acidophilus*, *Enterococcus faecium*) for a duration of 15 days, as Ettore was required to take antibiotics for medical purposes. The remaining therapy was based on the prescribed melatonin and CBD. During the follow-up, six months after the initiation of integrated and interdisciplinary therapy, the female caregiver indicated that Ettore appeared significantly calmer and more manageable. Additionally, regarding the issue of frustration, they noted a marked improvement, as he had ceased to exhibit destructive behaviors. At this point, the therapy plan was stabilized to: melatonin (1 tablet twice daily) and CBD 10 % full spectrum (1 drop in the morning and 1 in the evening). After 6 further months of stable treatment, the positive clinical condition was maintained at follow-up.

Discussion

This case report elucidates the intricate therapy of behavioral disorders in high-driving dogs, exemplified by the Lagotto Romagnolo (working dogs). The caregivers noticed a worsening of behavior following the interruption of the routine, and a decrease in social interaction due to the new employment of the female caregiver. The widespread hyperactivity, heightened social vigilance, and engagement in displacement behaviors (such as spinning and scratching) indicate an underlying intermittent anxious state (Masson et al., 2024). Anxiety has been significantly increased by frustration (Casey et al., 2022) resulting from excessive stimulation, such as excessively long walks (up to 15 km) and performative olfactory games in the woods, which probably intensified his state of excitement rather than alleviating it. The destructive behaviors were systematically recognised as reinforcement-maintained attention-seeking behaviors, indicating that the caregivers' response, regardless of its negativity, functioned as an unintentional form of positive reinforcement (Landsberg et al., 2013). Therefore, modifications to the environment and daily routines—such as the establishment of a consistent and predictable routine, the minimization of stimulating factors, and the incorporation of calming recreational activities—have been prescribed as a fundamental aspect of therapy. Such measures are essential for high-energy dogs exhibiting hyperactivity and frustration, as demonstrated by Casey et al. (2022), since environmental clarity and the restriction of non-functional stimuli are critical for mitigating chronic arousal and social vigilance.

The combined effect of melatonin and CBD full-spectrum has been crucial for symptom relief and the regulation of the neuroendocrine axis. CBD, through its interaction with the endocannabinoid system, has been utilized for its anxiolytic effects, as well as to enhance overall satisfaction and increase patient well-being (Di Salvo et al., 2023), alleviating discomfort and feelings of frustration and the trouble in calming (Marliani et al., 2024). Concurrently, melatonin was utilized for its established mood-stabilizing properties and for the control of excitement (Salavati et al., 2023; Song et al., 2025). As evidence of their combined positive effects, Sacchettino et al. (2023a) published a case report concerning a 5-year-old mixed-breed dog afflicted with a compulsive behavior unresponsive to conventional antidepressant treatments. The researchers utilized

an interdisciplinary and integrative methodology that incorporated three elements: a behavioral program, the administration of cannabis products, and melatonin supplementation (2 mg/day). Clinical observations and caregivers reports suggested that the integrated strategy led to a reduction in the frequency of compulsive episodes and enhanced overall management of the dog compared to previous therapy with paroxetine, with no short-term side effects noted. The authors noted that maintaining a reduction in dysfunctional behavior to a level considered acceptable by caregivers was achieved during a subsequent four-month follow-up period. Thus, it is likely that the combined melatonin-CBD treatment of our patient effectively regulated arousal, utilizing the synergistic effects of both substances for emotional stabilization.

The end of undesirable behaviors in the initial months was directly attributable to the effective application of involuntary reinforcement management (Landsberg et al., 2023). By removing all forms of caregiver attention, including reprimands, and promptly diverting the dog to suitable calming activities, such as a Kong, the reinforcement loop was disrupted. This suggests that the damaging activity was not compulsive but rather instrumental and part of an ineffective coping strategy for frustration.

The administration of psychobiotics was crucial, especially considering the patient's medical history of recurrent gastroenteritis episodes and antibiotic use; lactobacilli-based probiotics offered continuous support to the emotional axis and dysfunctional behaviors (Yeh et al., 2022; Bijaoui&Zimmerman, 2025), in addition to the recolonization of the intestinal microbiota after antibiotic treatment. This underscores the important and interrelated functions of intestinal health, inflammation, and the gut-brain axis in the manifestation and treatment of canine behavioral disorders (Gorzelanna & Miszczak, 2024; Kielbik & Witkowska-Piłaszewicz, 2024).

Conclusion

This clinical case study described the response to the one-year integrated treatment given to a Lagotto Romagnolo who was diagnosed with an intermittent anxiety status and chronic frustration. The enduring remission of clinical symptoms was not solely attributable to the administration of melatonin and CBD but rather to the concurrent stabilization of various components. Although integrated neuro-emotional support provided the necessary physiological basis, the key to success lies in the rigorous implementation of behavioral prescriptions. The implementation of attention management and the reduction of excitatory activities were essential in disrupting the negative learning cycle that perpetuated destructive and hyperactive behaviors. This, along with the management of the chewing ritual and the support of the gut-brain axis, facilitated the transformation of the dog's environment and relational routine. This clinical case supports a model wherein pharmacological or nutraceutical therapy does not replace behavioral and environmental modifications but serves as a catalyst that reduces the patient's arousal, enhancing receptivity to learning and facilitating relational changes and routine consolidation into sustained clinical remission.

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Integrare l'asse intestino-cervello, il CBD e la melatonina nella gestione dell'ansia e dei comportamenti disfunzionali guidati dalla frustrazione in un Lagotto Romagnolo: un caso clinico in approccio integrato

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Sintesi

Ettore, un Lagotto Romagnolo maschio di due anni e mezzo, è stato sottoposto a una visita comportamentale a causa della difficoltà a mantenere la calma in casa in presenza della sua caregiver. I sintomi manifestati, quali iperattività, richieste costanti di interazione e comportamenti di distruzione, sono stati interpretati come l'espressione di un'ansia sottostante esacerbata da una frustrazione cronica, tipica dei cani da lavoro. L'insorgenza è coincisa con una modifica degli orari della caregiver e una sua ridotta disponibilità. Il protocollo terapeutico ha integrato melatonina e cannabidiolo (CBD) per i loro effetti ansiolitici e di potenziamento del benessere, affiancati da un supporto mirato per l'asse intestino-cervello, insieme a un intervento di modificazione comportamentale e ambientale specifico. I follow-up successivi hanno mostrato una significativa diminuzione dell'irrequietezza e un aumento dell'autonomia, convalidando l'efficacia di una strategia di gestione multimodale che incorpora terapia farmacologica, supporto emotivo e attenzione alla salute intestinale.