



An Investigation of the Physiological Effects of Animal-Assisted Therapy on Stress and Well-Being in End-Stage Cancer Patients: Examination of Brain Hormone Promotion

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Abstract

The present study investigated the physiological effects of animal-assisted therapy (AAT) on stress reduction and well-being of terminal cancer patients, focusing on the autonomic nervous system activity and brain hormone promotion. With the global increase in cancer incidence and mortality, especially among the elderly, palliative care with emphasis on the patients' quality of life (QOL) is essential. AAT, involving trained therapy dogs, reportedly promotes relaxation, reduces stress, and improves mental health, but objective evidence in terminal patients remains limited.

In this cross-sectional study conducted at a hospice from April 2022 to February 2023, 35 terminal cancer patients who liked dogs participated. A heart rate variability (HRV) analysis was performed to assess the autonomic nervous system changes, measuring the low frequency (LF)/high frequency (HF) ratio and HFnu as indicators of sympathetic and parasympathetic activities, respectively. Salivary cortisol levels, a stress marker, and subjective measures, including visual analog scale (VAS) scores, were also recorded before and after the 10-minute AAT sessions. The therapy involved interaction with trained therapy dogs, with the patients freely engaging through touching, talking, or simply being near the animals.

Our results showed significant decreases in the LF/HF ratio and salivary cortisol levels, alongside increases in HFnu, indicating enhanced parasympathetic activity and relaxation. Subjectively, patients reported reduced stress and improved mood post-AAT. These findings suggest that AAT stimulates the release of happiness-related neuropeptides, including endorphins and oxytocin, which contribute to stress alleviation and emotional well-being. The activation of the reward pathways and reduction of stress hormones support the physiological basis for AAT's benefits in terminal care.

In conclusion, dog-assisted therapy effectively promotes relaxation and reduces stress in terminal cancer patients by modulating autonomic function and neurohormone secretion. Repeated animal interactions may sustain these benefits, improving the patients' QOL during end-of-life care. Further research with larger samples and control groups is needed to confirm its long-term effects and optimize the therapeutic protocols.

Keywords: Alternative Therapy; Palliative Care; End of Life; Cancer Patients; Animal Assisted Therapy

Abbreviations

AAT: Animal-Assisted Therapy; QOL: Quality of Life; HRV: Heart Rate Variability; LF: Low Frequency; HFnu: Normalized High-Frequency Component; VAS: Visual Analog Scale; WHO: World Health Organization; ECG: Electrocardiogram

Introduction

Background

Recently, the global incidence of cancer and associated mortality rates have demonstrated a concerning upward trend. The International Agency for Research on Cancer, an esteemed research body affiliated with the World Health Organization (WHO), compiles comprehensive statistics on cancer incidence and mortality across 185 countries worldwide. According to these data, in 2018, approximately 18.1 million new cancer cases were diagnosed, and 9.6 million individuals succumbed to the disease, reflecting a considerable increase compared to previous estimates [1].

Japan, as a developed nation, bears a substantial cancer burden, with nearly half of its population expected to be affected during their lifetime—approximately 65% of men and 50% of women. It is projected that 26.7% of men (roughly one in four) and 17.8% of women (approximately one in six) will ultimately die from cancer [2]. On a global scale, the highest cancer mortality rates were observed in Hungary, followed by Croatia, in 2023 [3]. The ongoing demographic shift toward an aging population has further contributed to the increasing number of cancer cases, with the American Cancer Society projecting that the total number of cancer survivors will reach approximately 35 million by 2050 [4].

The advancements in early detection and therapeutic interventions have resulted in increased survival rates; however, challenges such as recurrence and metastasis often impede complete remission, ultimately leading to end-of-life stages and mortality [5]. In low-income countries, limited access to early diagnostic and treatment services results in comparatively lower reported incidence rates but higher mortality rates.

For instance, in Ethiopia, the incidence of breast cancer is approximately 60% lower than that in the United

States (40 per 100,000 versus 60 per 100,000), yet the mortality rate from breast cancer is twice as high (24 per 100,000 versus 12 per 100,000) [5]. The WHO underscores the importance of integrating cancer treatment with palliative care, with the aim of alleviating suffering and enhancing the patients' QOL across all stages of disease management [4]. Promptly initiating palliative care after diagnosis remains a critical global health priority.

Complementary and alternative therapies, including relaxation techniques, reportedly mitigate psychological distress, thereby reducing physical pain and promoting patient comfort [6,7]. Developing effective supportive interventions that address mental suffering—closely intertwined with physical symptoms—can considerably improve the palliative care outcomes.

For terminal cancer patients, the inevitability of death and progressive escalation of symptoms necessitate a focus on optimizing QOL within the palliative care frameworks [8]. If relaxation techniques can effectively reduce stress, they may also diminish psychological suffering, consequently alleviating physical pain and ultimately leading to improved QOL for patients.

One promising complementary approach is animal-assisted therapy (AAT). AAT involves the therapeutic use of animals under the supervision of healthcare professionals, with the goal of promoting recovery of daily rhythms, emotional stability, autonomy, motivation, social skills, and overall independence—thereby enhancing QOL [9,10]. AAT reportedly is associated with relaxation induction and stress reduction, with reported benefits including lowered blood pressure, stabilized circulatory dynamics [11–13], improved mental health [14], pain relief [15,16], and reductions in the symptoms of depression and anxiety [17–21]. Notably, AAT has demonstrated efficacy in alleviating various types of pain, including cancer-related pain, and fostering physical and mental relaxation [22,23].

Despite these encouraging findings, the body of research remains limited in terms of quantitative data supporting the objective evaluation of the effects of AAT. A previous systematic review has identified challenges and uncertainties regarding the strength of evidence supporting AAT's efficacy [24], and the specific benefits of AAT for end-of-life cancer patients require further rigorous investigation.

Purpose

The prefrontal cortex constitutes a considerable portion of the brain's frontal lobe and is responsible for various higher-order mental functions, including cognition, memory, emotional regulation, and behavioral inhibition. The higher functions of the prefrontal cortex are supported by neurotransmitters, including dopamine, serotonin, norepinephrine, and gamma-aminobutyric acid. Animal interactions promote relaxation and a sense of security. Additionally, endogenous opioids, such as endorphins, are produced within the brain and exhibit effects similar to those of morphine. These neuropeptides are predominantly distributed within the brain's reward system, and their secretion can reduce stress, alleviate pain, and induce feelings of happiness. Contact with animals reportedly can stimulate endorphin secretion. However, to date, there has been no objective investigation into whether the changes in autonomic nervous system activity-potentially influenced by AAT-affect the brain hormones in terminal cancer patients. Therefore, the present study aimed to examine the effects of AAT on the autonomic nervous system activity and the subsequent promotion of brain hormones, thereby elucidating its relaxing and neurochemical effects in this patient population.

Materials and Methods

Study design and setting

The present research employed a cross-sectional (observational) study design with a non-randomized comparative approach. The investigation was conducted at a single hospice facility, with the data collection period spanning from April 2022 to February 2023.

Survey

The participants were adult individuals who were deemed suitable to receive AAT by physicians, specifically end-of-life cancer patients who expressed a preference for dogs. Prior to study participation, the researchers provided an explanation of AAT and obtained informed consent from each participant. The exclusion criteria included patients with a history or current diagnosis of orthostatic hypotension, diabetes mellitus, and Parkinson's, cerebrovascular, and cardiovascular diseases. Additionally, patients using narcotics, those with decreased salivary secretion, or those with altered states of consciousness were excluded. If any of these conditions arose during the course of the study, the participant was withdrawn from the study, and the intervention was discontinued for that individual.

The hospice where the study was conducted permanently housed one handler and two therapy dogs. AAT was performed within the facility using trained therapy dogs that could be handled by the handlers. The therapy dogs underwent daily health checks, regular veterinary examinations, vaccinations, and other necessary procedures to eliminate the risk of zoonotic infection. The therapy dogs included a Labrador Retriever (a large breed) and a Cavalier King Charles Spaniel (a small breed). The participants were free to choose which therapy dog they preferred to interact with. Communication between the participants and handler was limited to necessary conversations. The participants voluntarily engaged with the therapy dogs, with the handler supporting their interactions based on the participants' condition and level of rest, following the physician's instructions to "observe," "speak," or "touch." The AAT sessions were conducted once daily between 10:00 and 14:00, lasting 10 minutes each, either at the bedside or in a designated space. According to the physician's instructions, all participants received the intervention through "touch" and performed the activity at the bedside.

The study protocol involved each participant undergoing two sessions, with the data collected during each session. The assessments included both objective and subjective measures, which are described below

- **Electrocardiogram (ECG):** The changes in R-R intervals were monitored at multiple time points immediately before AAT, at 2, 5, 7 minutes during, immediately after, and at 30 minutes, 1 hour, and 2 hours post-intervention. The ECG data were obtained using the Active Tracer AC-301A device (GMS Co., Ltd. Japan), which recorded the R-R intervals and analyzed their spectral components. The electrodes were attached to three points on the chest, transmitting data wirelessly to the monitoring device, thereby ensuring no physical intrusion or restriction of movement during the measurement.
- **Salivary cortisol:** Saliva samples were collected once on the day prior to the AAT and during the intervention period at 9:00 and 16:00. To determine the stress levels, we measured the salivary cortisol concentrations, utilizing the SOMA cube reader (MP JAPAN CO., LTD.) with swabs inserted sublingually. The color change of the swab indicated sufficient saliva absorption, and measurements were performed with dedicated equipment.

- **Mood:** Mood changes were assessed using the VAS immediately before and after each AAT session. The participants marked their current mood on a 10 cm line, providing a quantitative measure of their emotional state.
- **Interviews:** Qualitative data were obtained through interviews with patients regarding their impressions of AAT and their feelings toward the therapy dogs, as well as communication with ward nurses.

The concept of “happiness hormones” refers to the neurochemical substances—serotonin, oxytocin, dopamine, and endorphins—secreted in appropriate amounts to promote psychological and physiological stability and well-being.

Serotonin, a neurotransmitter primarily located in the basal nuclei, raphe nuclei, and hypothalamus, regulates the secretion of other neurotransmitters, including dopamine and norepinephrine, which are associated with pleasure, joy, anxiety, and fear. Adequate serotonin levels help stabilize mood and prevent symptoms of depression, insomnia, and panic disorders.

Oxytocin, which is secreted from the hypothalamus, plays a role in enhancing trust and empathy, as well as alleviating anxiety and fear. It is released through physical contact, such as hugging or hand-holding, and social interactions.

Dopamine activates the brain’s reward system, contributing to feelings of pleasure. Its secretion is stimulated by rewarding stimuli, including substances such as alcohol and drugs, which can lead to dependency.

Endorphins, which are endogenous opioids, produce analgesic and euphoric effects, similar to the effects of morphine. Beta-endorphins, in particular, have potent pain-relieving properties and are involved in phenomena such as “runner’s high.” They are released during activities, such as exercise, listening to music, laughter, romantic interactions, and enjoying delicious food, contributing to positive mood and stress reduction.

Analyzing the autonomic nervous system changes can provide insights into the relaxation effects of AAT. If such changes are observed—specifically, increased secretion or promotion of these “happiness hormones”—it would serve as evidence of the neurochemical mechanisms underlying relaxation. Furthermore,

these findings would support the efficacy of AAT by demonstrating its influence on the neurophysiological pathways associated with well-being.

Statistical analysis

In the present study, the patients who died within 1 week of the assessment were excluded. Additionally, during the investigation, many patients experienced difficulties in saliva collection or deterioration of their general condition, which, despite their cooperation, considerably reduced the number of participants suitable for analysis. Consequently, the analysis was conducted on 35 terminal cancer patients who could undergo salivary cortisol concentration measurements twice, and the mean values from these two measurements were used for statistical testing. The analysis compared autonomic nervous system activity changes, salivary component variations, and VAS score changes across each respective item. Given that all patients expressed a desire to undergo AAT and considering the terminal stage context with an emphasis on dignity, a control group could not be established.

First, the autonomic nervous activity was evaluated via HRV analysis. This analysis involves examining the temporal fluctuations of the HR to assess the balance between the sympathetic and parasympathetic nervous system activities. The following two key indices were emphasized: the LF/HF ratio, with LF corresponding to the 0.04-0.15-Hz band and being primarily associated with sympathetic nervous activity and HF corresponding to the 0.15-0.4-Hz band and reflecting parasympathetic activity. The LF/HF ratio provides an index of the autonomic balance, with a higher ratio indicating sympathetic dominance and a lower ratio suggesting parasympathetic dominance.

Second, the normalized high-frequency component (HFnu), calculated as HF divided by the total power spectrum (LF + HF) and expressed as percentage ($HFnu = HF / [LF + HF] \times 100$), was used. HFnu indicates the relative strength of the parasympathetic nervous system activity. A higher HFnu suggests parasympathetic dominance. Meanwhile, a lower HFnu represents sympathetic dominance. In this study, HFnu was measured due to the significant variability observed in HF values within individual patients. Considering that such fluctuations are common, data normalization for analysis is an established approach in autonomic nervous system research. Hence, HFnu is a suitable metric.

Regarding ECG analysis, the ECG signals obtained using the ECG measurement device were subjected to spectral analysis with the frequency analysis software (Mem Calc/Win2.0; GMS Co., Ltd.). The R-R interval time series was analyzed to extract spectral components, particularly LF/HF and HF values, with HF further normalized to obtain HFnu. Frequency analysis of ECG results involves power spectral analysis of the R-R interval time series to evaluate autonomic function. The LF component reflects sympathetic nervous system activity, which increases under psychological stress. Meanwhile, the HF component indicates parasympathetic nervous system activity associated with relaxation. The LF/HF ratio is considered an indicator of stress, as it captures the relative dominance of sympathetic over parasympathetic nervous system activity, regardless of whether what activity is predominant. Cortisol is a well-established biomarker of stress. Thus, to evaluate stress levels, salivary cortisol levels were measured using a stress marker analysis device.

All data obtained from the investigation were analyzed using the Statistical Package for the Social Sciences software version 23 (IBM Inc.). The data were subjected to non-parametric statistical tests. The Wilcoxon signed-rank test was used for comparisons conducted before and after AAT, and the Friedman test was used to analyze changes over time ($p < 0.05$).

Ethics

This study was approved by the Institutional Review Board (3002-2, 2022004) and was supported by Grants-in Aid for Scientific Research (19K10884). The researchers provided clear explanations to the participants regarding the nature of the investigation. Further, they obtained informed consent after

explaining the management of information, confidentiality obligations, and procedures for information disclosure. The patient’s dignity and rights were also taken into consideration, as the patient was in the terminal stage. Ethical considerations for the dogs used were also taken into account in accordance with the Animal Welfare Act, with due consideration given to the animals’ physical condition and rest.

Results and Discussion

Results

The breakdown of the participants was 18 women and 17 men. The age groups were 4 in their 60s, 15 in their 70s, 13 in their 80s, and 3 in their 90s. The diseases they had were lung cancer, liver cancer, colon cancer, stomach cancer, kidney cancer, and pancreatic cancer.

During the implementation of AAT, the patients exhibited active behaviors such as petting, touching, and talking to dogs. Throughout the AAT sessions, the patients remained in contact with the dogs by keeping their hands on the animals’ bodies. The therapy dogs exhibited active behaviors, including closely snuggling alongside the patients on the bed, rubbing against them, and maintaining eye contact. Interviews with the patients revealed exclusively positive comments, such as healing and enjoyable time, and negative remarks were not expressed.

Initially, the maximum, minimum, and average values of the following parameters were calculated: LF/HF ratio, HF, HFnu, salivary cortisol levels, and VAS scores. Table 1 shows the mean LF/HF ratio, HFnu, salivary cortisol levels, and VAS scores (Table 1).

	Before AAT	2 min	5 min	7 min	After AAT	...	30 min	...	1 h		2 h
LF/HF ratio	4.82	2.92	2.78	3.88	2.62	...	1.71	...	3.14		4.32
HFnu	25.30	57.23	37.72	35.88	60.93	...	61.09	...	54.79		54.66
Salivary cortisol levels	14.29	-	-	-	8.37		-		-		-
VAS score	6.0	-	-	-	7.3		-		-		-

Table 1: Average value for each parameter.

The maximum, minimum, and mean LF/HF ratios before AAT were 57.00, 0.14, and 4.82, respectively. During AAT, the maximum values were 14.73 at 2 min, 21.14 at 5 min, and 15.85 at 7 min. Meanwhile, the minimum values were 0.09 at 2 min, 0.20 at 5 min, and 0.12 at 7 min. The mean LF/HF ratios during the respective time points were 2.92, 2.78, and 3.88. After AAT, the maximum, minimum, and mean LF/HF ratios were 11.34, 0.21, and 2.62, respectively. At 30 min after AAT, the maximum, minimum, and mean values were 13.80, 0.33, and 1.71, respectively. At 1 h after AAT, the maximum, minimum, and mean values were

15.55, 0.16, and 3.14, respectively. At 2 h after AAT, the maximum, minimum, and mean values were 58.12, 0.12, and 4.32, respectively. Notably, the LF/HF ratio was lowest at 30 min after AAT, and an increase nearing pre-AAT levels was observed at 2 h after AAT. The Friedman's test revealed a significant decrease in the LF/HF ratio from the start of AAT to 2 h after AAT ($p < 0.05$) (Figure 1).

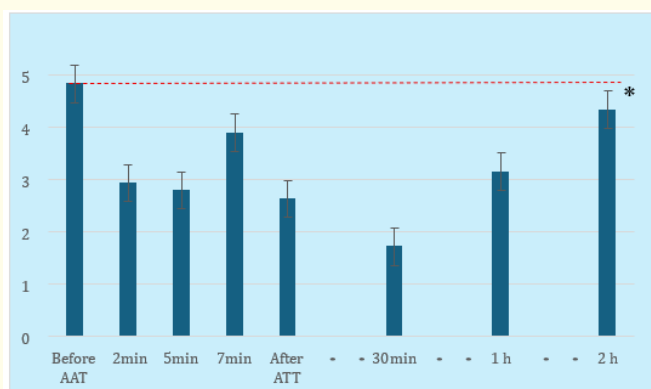


Figure 1: Time series changes in LF/HF.

Friedman's * $p < 0.05$ ($n = 35$).

Before AAT, the maximum, minimum, and average values of the high-frequency component (HF), which is an indicator of relaxation, were 1268.06, 1.06, and 180.19 ms^2 , respectively. During AAT, the maximum values were 1753.94 ms^2 at 2 min, 1601.92 ms^2 at 5 min, and 1238.13 ms^2 at 7 min. Meanwhile, the respective minimum values were 4.76 ms^2 , 0.71 ms^2 , and 0.58 ms^2 . The mean values at 2, 5, and 7 min were 328.98, 228.06, and 163.20 ms^2 , respectively. After AAT, the maximum, minimum, and mean values were 1930.15, 1.06, and 311.66 ms^2 , respectively. At

30 min after AAT, the maximum, minimum, and mean values were 2006.22, 2.88, and 412.04 ms^2 , respectively. At 1 h after AAT, the maximum, minimum, and mean values were 1942.50, 1.20, and 334.59 ms^2 , respectively. At 2 h after AAT, the maximum, minimum, and mean values were 1674.27, 0.80, and 209.05 ms^2 , respectively. The HF values increased significantly from 2 min during AAT to 2 h after AAT. The Friedman's test indicated a significant increase in the HF values ($p < 0.001$). To ensure the reliability of the HF data, the normalized HF (HFnu) was also calculated. The maximum, minimum, and average HFnu values before AAT were 60.39, 5.39, and 23.34, respectively. During AAT, the maximum values were 92.25 at 2 min, 95.09 at 5 min, and 87.88 at 7 min. Meanwhile, the respective minimum values were 7.35, 7.25, and 11.82. The mean HFnu values at 2, 5, and 7 min were 58.40, 35.59, and 33.06, respectively. After AAT, the maximum, minimum, and mean values were 87.20, 10.88, and 61.83, respectively. At 30 min after AAT, the maximum, minimum, and mean values were 87.03, 23.74, and 60.36, respectively. At 1 h after AAT, the maximum, minimum, and mean values were 93.17, 17.20, and 56.67, respectively. At 2 h after AAT, the maximum, minimum, and mean values were 89.36, 23.02, and 55.51, respectively. The HFnu also showed a significant increase from 2 min during AAT to 2 h after AAT ($p < 0.001$) (Figure 2).

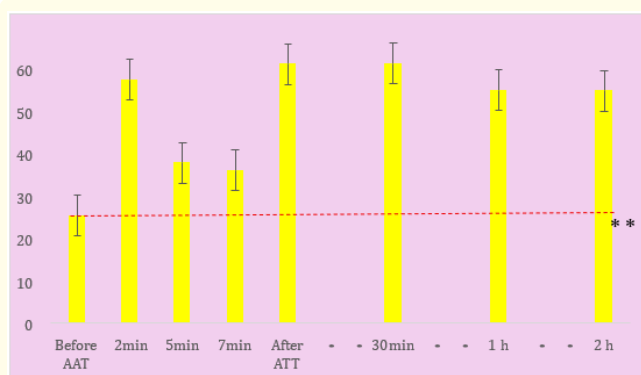


Figure 2: Time series changes in HFnu.

Friedman's ** $p < 0.01$ ($n = 35$).

The maximum, minimum, and mean salivary cortisol levels before AAT were 40.00, 1.30, and 14.29 $\mu\text{g/dL}$, respectively. The maximum, minimum, and mean salivary cortisol levels after AAT were 38.3, 1.0, and 8.37 $\mu\text{g/dL}$, respectively. The Wilcoxon signed-rank test revealed a significant decrease in the salivary cortisol levels after AAT ($p < 0.05$) (Figure 3).

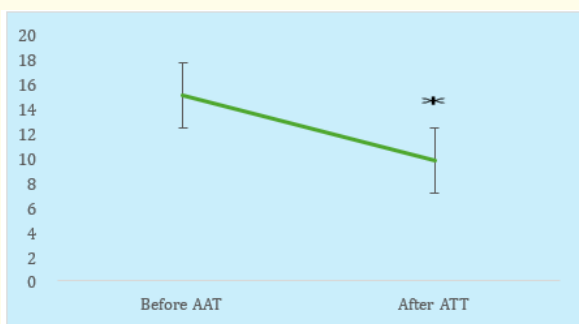


Figure 3: Changes in salivary cortisol levels before and after AAT.

Wilcoxon $p < 0.05$ ($n = 35$).

The maximum, minimum, and mean VAS (cm) scores before AAT were 9.1, 1.1, and 6.0, respectively. Meanwhile, the maximum, minimum, and mean VAS (cm) scores after AAT were 10.0, 4.0, and 7.3, respectively. The Wilcoxon signed-rank test indicated a significant reduction in the VAS scores after AAT ($p < 0.05$) (Figure 4).

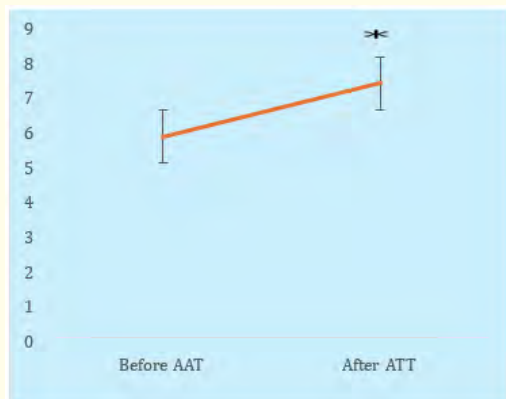


Figure 4: Change in VAS score before and after AAT.

Wilcoxon $p < 0.05$ ($n = 35$).

Discussion

This study aimed to objectively examine the stress-reducing effects of AAT involving dogs in patients with terminal-stage cancer by analyzing changes in autonomic nervous system activity and associated neurohormonal responses. This investigation included several measures: the frequency components of heart rate variability in the R-R interval time series—particularly LF/HF ratio and HF (HFnu)—which are physiological indicators; salivary cortisol level, which is a biochemical marker; and VAS scores and interview responses, which are subjective parameters. The significant changes observed across these parameters showed that AAT facilitates the secretion of neurohormones within the brain. Further, the physiological data indicated that hormone secretion contributed to alleviating psychological distress experienced by patients with terminal-stage cancer.

Regarding changes, the HFnu, which is a relaxation indicator, significantly increased during AAT compared with pre-AAT conditions. This finding indicated a relaxation effect associated with neurohormonal promotion. The LF/HF ratios from the start to the end of AAT significantly decreased, thereby further supporting this conclusion. Salivary analyses conducted before and after AAT showed significant increases. Based on this finding, AAT enhances neurohormonal secretion, thereby reducing stress in patients with terminal-stage cancer. Collectively, these findings confirmed that AAT promotes neurohormonal activity, which plays a role in stress mitigation.

Patients with terminal-stage conditions are acutely aware of their limited lifespan. Further, they live with ongoing symptoms such as cancer-related pain, comorbidities, and declining physical functions, which contribute to overall existential suffering. Under these circumstances, AAT exerts a substantial calming effect, which significantly reduces stress. Considering that patients with terminal-stage cancer often have profound feelings of life's preciousness and that engagement with animals can be considered a type of entertainment within hospital settings, AAT is particularly effective for patients who have an affinity for dogs.

Subjectively, during AAT and interviews, the patients expressed positive comments toward the dogs and exhibited behaviors indicating a desire to interact, such as touching and petting. Previous studies have shown that AAT can induce relaxation, reduce pain,

and decrease discomfort, as supported by data collected during interviews and questionnaire surveys, by diverting attention from pain sensations and promoting emotional well-being.

The prefrontal cortex, which occupies a significant portion of the frontal lobe, governs higher-order functions including cognition, memory, emotional regulation, and behavioral inhibition. Its activity is supported by neurotransmitters such as dopamine, serotonin, norepinephrine, and gamma-aminobutyric acid. Interaction with animals promotes relaxation and a sense of security by activating the prefrontal cortex.

The reward system involves increased dopamine secretion, which promotes feelings of pleasure and happiness. This system comprises neural circuits involving the ventral tegmental area and nucleus accumbens, where dopamine produced in the ventral tegmental area is released into the nucleus accumbens and projected to the prefrontal cortex, thereby influencing the amygdala and contributing to reward sensations.

The endocrine system also plays a role, specifically via the secretion of oxytocin from the posterior pituitary gland in the hypothalamus. Oxytocin is associated with feelings of happiness and is further released through skin-to-skin contact with animals. Elevated oxytocin levels can suppress cortisol secretion from the adrenal cortex, thereby reducing stress responses. In addition, endogenous opioids, such as endorphins, are produced within the brain and have morphine-like effects. They are widely distributed throughout the reward pathways and contribute to stress reduction, analgesia, and feelings of well-being. Interaction with animals has been found to stimulate endorphin release.

Based on these mechanisms, neurochemical mediators—including serotonin, dopamine, oxytocin, and endorphins—are involved in the therapeutic effects of animal-assisted interventions, with endorphins playing a particularly important role. Contact with animals increases oxytocin secretion, which indirectly promotes endorphin release, thereby enhancing feelings of happiness and relaxation. This interaction results in stress relief and relaxation, partly by lowering cortisol levels. The promotion of endorphin secretion via AAT has been associated with positive effects on mental and physical health. According to the findings of this study, AAT significantly contributes to reducing stress and enhancing well-being in patients with terminal-stage cancer.

Further, repeated exposure to AAT may produce synergistic effects, sustaining relaxation over longer periods. Repeated stimulation activates the brain's reward system, potentially increasing stress tolerance. Autonomic nervous system activity remained significantly altered up to 2 h after AAT, indicating that repeated sessions could prolong these benefits. Regular interactions with dogs may improve autonomic balance, elevate baseline stress levels, and extend relaxation effects.

In addition, habitual engagement in animal contact can suppress the secretion of stress hormones, such as cortisol. Increasing the frequency of interactions—such as daily short sessions—may yield more sustained benefits than infrequent or brief encounters. The long-term regulation of the central nervous system involves the control of autonomic functions by the hypothalamus, influenced by limbic system emotions. Serotonin, a key neurotransmitter, contributes to mood stabilization and happiness. In particular, serotonin levels increase during emotional experiences, such as touching animals and engaging in emotionally stimulating activities. Long-term effects are likely mediated by activities that activate the parasympathetic nervous system and increase serotonin secretion, and by the regulation of reward pathways involving dopamine and endorphins, and stress response systems such as the amygdala and hypothalamic–pituitary–adrenal axis. Neuroplastic changes may occur, leading to reduced stress reactivity.

The current study had several limitations. For example, it had a small sample size, particularly in patients with mid- to late-stage terminal illness, due to their deteriorating condition and declining physical functions. The absence of a control group, the lack of long-term follow-up, and the need to validate the cumulative effects of repeated interventions remain a challenge in future research.

Conclusion

AAT effectively reduces stress and enhances well-being in patients with terminal-stage cancer. Physiologically, AAT was found to promote the secretion of happiness-related neurohormones such as endorphins and oxytocin, thereby restoring autonomic balance. In addition, the cortisol levels of the patients decreased, indicating a relaxation response. AAT also alleviated psychological distress and improved mood, thereby contributing to better mental stability and quality of life in patients with terminal illness. Repeated interactions with dogs may further sustain these beneficial effects over time.

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Conflict of Interest

No Conflict of interest.

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