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1 **Abstract**

2   The demand for mental health support systems has been increasing because of the rising prevalence of mental

3 health issues globally. These challenges related to mental health have been addressed through animal-assisted

4 intervention. This approach has gained recognition as an effective method that enhances emotional stability and

5 fosters social bonds. Canine-assisted intervention, a subset of animal-assisted intervention that involves dogs, is

6 recognized for its effectiveness in managing stress and depression in humans. Despite the development of various

7 canine-assisted intervention programs, there is insufficient scientific data evaluating the efficacy of each program.

8 Customized programs that target individuals' symptoms and needs are necessary to effectively manage stress and

9 depression. As such, generalizing the effects of canine-assisted intervention across diverse situations continues to be

10 a challenge. This review aims to identify the most effective canine-assisted intervention programs for various target

11 groups and suggest strategies that maximize the effects of canine-assisted intervention programs by consolidating

12 various biometric indicators and physiological evaluation tools and by analyzing the effects of canine-assisted

13 intervention through multiple approaches. It examines current studies demonstrating how interactions with therapy

14 dogs lead to remarkable psychological and physiological changes, including measurable reductions in stress

15 indicators (such as cortisol levels and heart rates) and notable improvements in overall mood and emotional well-

16 being. Furthermore, this paper evaluates the effectiveness of canine-assisted intervention in various settings,

17 highlighting its potential as a therapeutic intervention and preventive measure in mental health care. Based on

18 previous findings, this review provides a comprehensive overview of the role of canine-assisted intervention in

19 enhancing human mental health and its potential for broader implementation across diverse environments.

20 Keywords: canine-assisted intervention, stress, depression, well-being

21

Introduction

Psychological and emotional crises, including stress and depression, have been rising significantly. They are closely associated with increasing suicide rates, posing a significant societal challenge on a broader societal level [1].

Addressing these crises necessitates more diverse and specialized support programs. For instance, animal-assisted intervention (AAI) has emerged as an effective approach to addressing these challenges [2]. It facilitates the development of emotional stability and social bonds through human-animal interactions. Such interactions are key to overcoming psychological crises [2-6]. AAI is a broad concept that includes all activities involving various animals in beneficial ways to enhance human health and welfare [7]. These interventions span multiple fields, including healthcare, education, and social welfare, thereby providing individuals with physical, psychological, social, and cognitive benefits [8]. Therefore, animal-related activities have been recognized for their contributions to helping enhance humans' psychological stability and social functions.

Canine-assisted intervention (CAI), a type of AAI, involves dogs during the intervention. It is categorized into three types: canine-assisted therapy (CAT), canine-assisted education (CAE), and canine-assisted activities (CAA) [9]. CAT is conducted by professional therapists, who integrate dogs into therapeutic processes to enhance cognitive, psychological, physical, or social functions. Their effectiveness has been demonstrated in adults and children with mental disorders or developmental disabilities [3]. CAE is a program that utilizes dogs to support children's educational achievement [9]. CAA is a broader concept that is not confined to structured, goal-specific programs. It is implemented in diverse settings and can be performed by both professionals and nonprofessionals [9].

An increasing number of studies have demonstrated the effectiveness of interventions such as CAT, CAE, and CAA in addressing mental health challenges. These interventions are specifically used as coping strategies for stress or depression [10-14]. However, further studies should be performed to more comprehensively understand the effects of CAI and determine its appropriate applications. Therefore, this paper examines the effects of CAI, specifically its impacts on stress and depression. This review also highlights the practical contributions of CAI-based mental health programs and offers valuable insights into their clinical practice and future research directions by evaluating the current state of CAI studies.

47 **CAI**

48   CAI offers unique advantages compared with general AAI. Unlike general AAI, CAI involves dogs that can form

49 strong bonds with humans and are particularly known for providing emotional stability. They are highly attuned to

50 human emotions, promoting positive interactions [15]. Additionally, they are versatile in a wide range of activities

51 because of their high intelligence and trainability; as a result, they can be trained for specific therapeutic goals [16,

52 17]. As such, their use in therapy provides comfort and familiarity, which can help enhance therapeutic outcomes

53 [18]. For example, reading programs that involve dogs help alleviate anxiety and nervousness among students with a

54 fear of public speaking [19].

55   Certain dog breeds are suitable for CAI because of their temperament, sociability, and trainability. The most

56 commonly selected dog breeds for therapy work include Golden Retrievers, Labrador Retrievers, Poodles, Pugs,

57 Cavalier King Charles Spaniels, and Beagles [20-22]. In a previous study, the suitability of different dog breeds for

58 therapy roles was evaluated using the Canine Behavior Assessment and Research Questionnaire; its results showed

59 that the most commonly used breeds for therapy by the Hokkaido Volunteer Dog Association are Labrador

60 Retrievers, Golden Retrievers, and Toy Poodles. Other breeds with calm and friendly temperaments may also be

61 effective as therapy dogs [23].

62 **CAI programs**

63   CAI programs consist of various forms categorized by target population, activity characteristics, and duration.

64 Specifically, target populations are categorized based on the human life cycle and provided with customized

65 programs. Individuals are categorized into three life stages: children (0–18 years), adults (19–64 years), and the

66 elderly (65 years and above) [24]. During childhood, they undergo rapid physical growth and brain development.

67 Their linguistic abilities, social skills, and emotional regulation abilities also develop during this time. Their

68 socialization processes and the formation of their self-identity are crucial. As such, their CAI programs should focus

69 on enhancing social skills and providing emotional support. During adulthood, adults need to maintain their physical

70 health and manage stress. They encounter various social responsibilities and relationships. They may also develop

71 mental health issues such as depression and anxiety. Therefore, their CAI programs should cover stress reduction

72 and mental health support initiatives. During old age, the elderly may experience chronic illness and decreased

73 physical functions. They may also feel isolated and lonely. Their risk of cognitive decline and dementia increases.

74 Thus, their CAI programs should include initiatives that reduce social isolation and activities that stimulate cognitive

75 functions [24, 25].

76   CAI programs can also be categorized based on the characteristics of their activities. They are divided into two

77 types: dynamic and static activities. Dynamic activities involve active physical movement and interaction. They aim

78 to enhance physical functioning, improve athletic abilities, and allow for energy expenditure. Their effects include

79 stress reduction caused by energy expenditure and the development of athletic abilities. Static activities focus on

80 promoting emotional exchange, stimulating cognitive abilities, and enhancing emotional well-being. For instance,

81 reading programs involving dogs effectively enhance a child's confidence. Additionally, incorporating dogs into

82 psychological counseling can reduce individual stress and anxiety. Each activity must be selected based on the age,

83 physical condition, and psychological needs of participants [26-31].

84   CAI can be categorized into two types based on duration: short- and long-term CAI [26]. Short-term CAI

85 programs last from a few minutes to a few weeks. They aim to alleviate temporary stress and provide immediate

86 emotional support. For instance, one-off CAI sessions can reduce anxiety and stress in students during exam periods

87 and offer a change of scenery for patients in hospitals [32-34]. Short-term CAI does not require complex planning or

88 long-term resource input and can be implemented in various environments. Long-term CAI programs last from a

89 few months to several years. They focus on encouraging long-term behavioral changes, providing continuous

90 emotional support, and achieving therapeutic goals [35]. For instance, individuals with mental health problems

91 undergo continuous therapy sessions and use CAI in rehabilitation therapy [36]. The effects of long-term CAI

92 include enhanced social skills, obtained treatment goals, and improved quality of life. Long-term CAI requires a

93 professional therapeutic plan with set goals; it also needs certified therapists and the continuous involvement of

94 experts [37].

95 Dog-mediated programs can be used for non-therapeutic activities to reduce stress, anxiety, and fear [38] and

96 improve the overall well-being of people [39]. For example, the presence of a dog in a classroom enhances the

97 concentration and motivation of students during classes [40]. Additionally, interactions with dogs remarkably reduce

98 stress among university students during midterm or final exams [41]. Therefore, CAI has been proven to be an

99 effective method for managing mental health issues such as anxiety, stress, and depression and for promoting overall

100 well-being [38-41]. The ability of dogs to provide emotional stability and their high trainability positively affect not

101 only therapeutic settings but also educational and non-therapeutic environments. With these benefits, CAI is a

102 valuable   alternative   approach   to   mental   health   care.

Stress in physiology

Stress is defined as a state of mental or emotional strain caused by adverse or demanding circumstances. A moderate amount of stress can help individuals perform daily activities. However, excessive stress can cause mental health problems, including anxiety disorders, depression, and panic disorders [42-44], accompanied by a range of negative emotions. Excessive stress can also lead to physical symptoms such as headaches, body aches, and sleep disturbances [42, 43]. Therefore, methods should be developed to manage stress efficiently.

Physiologically, stress affects various body systems, including the nervous, endocrine, and immune systems, and is not limited to emotional responses. When stressors are present, the neuroendocrine system triggers the release of stress hormones such as cortisol and adrenaline. Cortisol, secreted by the adrenal cortex, increases blood sugar levels to provide quick energy and suppresses immune functions to reduce inflammation. Its secretion is regulated by the hypothalamic–pituitary–adrenal (HPA) axis [45, 46]. Adrenaline and noradrenaline, secreted by the adrenal medulla, increase heart rate and blood pressure to prepare the body for a "fight-or-flight" response. Their secretion is regulated by the sympathetic–adrenal–medullary (SAM) axis [47].

Stressors induce the secretion of corticotropin-releasing hormone, which stimulates the release of adrenocorticotropic hormone (ACTH) from the anterior pituitary gland. ACTH stimulates the adrenal cortex and increases cortisol secretion. Cortisol enhances energy supply by increasing blood sugar levels and promoting protein and fat breakdown. Additionally, it maintains homeostasis through negative feedback mechanisms that regulate hormone secretion from the hypothalamus and pituitary gland [48].

Although cortisol plays an important role in acute stress, chronic stress results in the overactivation of the HPA axis and induces the excessive secretion of cortisol. A chronic increase in cortisol levels may elicit negative effects, such as decreased immune function, metabolic disorders, and increased risk of cardiovascular disease [49, 50]. Chronic stress can also contribute to depression and anxiety disorders. It induces constant adrenaline and noradrenaline secretion through the SAM axis, causing symptoms such as increased heart rate, increased blood pressure, and hypervigilance [47].

Because of these negative effects, the importance of stress management is emphasized. Meditation, exercise, psychological counseling, and social support networks can alleviate stress and improve physical and psychological health [51, 52]. Additionally, CAI is recognized as an effective method for managing stress [53].

130 **Measurement of stress levels**

131   Various physiological and psychological indicators can be used to evaluate stress levels. Accurate and objective

132 assessment requires multiple methods. The main assessment methods used are enzyme-linked immunosorbent assay

133 (ELISA) for cortisol, functional magnetic resonance imaging (fMRI), Hematological analysis for the

134 neutrophil/lymphocyte ratio (NLR), electroencephalogram (EEG), heart rate variability (HRV), and self-report

135 measures. Each method assesses different aspects of stress responses.

136   ELISA is a precise analytical technique used to quantitatively measure specific protein or hormone

137 concentrations in biological samples. In studies on stress, ELISA is primarily used to evaluate cortisol levels.

138 Cortisol, a major hormone that responds to stress, can be measured in the blood, saliva, and urine [46]. Cortisol

139 levels obtained through ELISA serve as reliable physiological indicators of stress levels [54]. ELISA can detect

140 small amounts due to its high sensitivity and specificity, and quick results can be obtained through relatively simple

141 experimental procedures. Because of these functions, it is widely utilized in clinical and research settings.

142   fMRI is a non-invasive imaging technology that visualizes activation patterns of the brain in real time. fMRI

143 measures blood oxygen level-dependent signals to indirectly detect changes in neural activity. In stressful situations,

144 fMRI can detect changes in the activation of brain regions such as the amygdala and prefrontal cortex. It can also

145 identify functional changes in specific regions and help understand stress-related neural circuits [55, 56]. It is mainly

146 used to study the physiological mechanisms of the brain involved in psychological stress [57]. However, it entails

147 high costs, requires specialized equipment that limits accessibility, and exhibits sensitivity to the movement of

148 subjects, imposing constraints on experimental conditions [56].

149   The NLR is used as an indicator of stress and inflammatory responses; it is calculated by comparing the levels of

150 neutrophils and lymphocytes in the blood [58]. Hematological analysis for the neutrophil/lymphocyte ratio (NLR) is

151 a technique that can quickly and accurately assess inflammation and stress responses. Although it is primarily used

152 in animal studies, it can also be applied to human stress research [59]. The NLR is useful for evaluating

153 physiological responses to stress because it increases under high-stress conditions [60]. It can be measured using

154 Hematological analysis to evaluate stress and inflammation through simple blood examinations, allowing for

155 immediate on-site results. Hematological analysis is a particularly cost-effective technique suitable for repeated

156 measurements.

157   Brain waves reflect the brain's overall activity and can be measured in real time through an EEG. They are

158 divided into five main types and appear in different states: Delta waves (0.5–4 Hz) appear in deep sleep, theta waves

159 (4-8 Hz) appear in shallow sleep or deep meditation, and alpha waves (8–13 Hz) appear in relaxed states. Beta

160 waves (13–30 Hz) are detected in concentration, cognitive work, and stress conditions, especially high beta waves

161 (20–30 Hz) reflecting stress-related neural activities. Gamma waves (30 Hz or higher) are associated with high-

162 dimensional cognitive functions and complex information processing. In stressful situations, beta waves increase

163 activity, particularly high beta waves. Through EEG, changes in brain waves can be detected to assess stress levels

164 [61].

165 The HRV measures the variation in time intervals between heartbeats, reflecting autonomic nervous system

166 balance and stress levels [61, 62]. Under stress, it decreases because of sympathetic nervous system activation. It is

167 non-invasive and easy to measure, making it widely used in stress-related research.

168 Self-report measures involve individuals personally assessing their stress levels. Common tools include the

169 Perceived Stress Scale (PSS) and the Visual Analog Scale (VAS) [63, 64]. These self-reports are simple and quick to

170 administer; therefore, they are suitable for large population studies.

171 **Effects of CAI on stress in the non-elderly**

172 CAI can be an effective method for reducing stress in humans. Various studies have demonstrated the beneficial

173 effects of CAI on stress across different age groups. For instance, CAI programs can be particularly beneficial for

174 addressing stress in children. A study has demonstrated that interactions with dogs during classes significantly

175 reduce stress levels in neurotypical and neurodivergent children requiring special educational care. For example,

176 children in the dog intervention group exhibited significant reduction in average salivary cortisol levels (pre-

177 intervention: M = .1482 μg/dL, SD = .05; post-intervention: M = .0853 μg/dL, SD = .02; t(8) = 4.157, p = .003, d =

178 1.39) compared with those in the control group, which exhibited no significant changes (pre-intervention: M = .1486

179 μg/dL, SD = .05; post-intervention: M = .1468 μg/dL, SD = .06; t(14) = .487, p = .634, d = .13) [10]. This result

180 suggests that dog interventions can attenuate stress levels in school children. Additionally, short-term interactions

181 with dogs significantly reduce stress levels and enhance the mobility and mood of children in pediatric critical care

182 and acute care units, suggesting the benefits of CAI application to highly stressed children.

183 For instance, children who participated in an AAI program demonstrated a significantly higher activity level 3

184 hours after the visit compared to children who did not participate (B = 9.825, SE = 3.760, p < .001; β = 0.689).

185 Moreover, mood levels improved significantly in the AAI group, as indicated by a strong interaction effect between

186   mood and group (F (1, 45) = 79.05, p < .001). Regarding stress levels, children in the AAI group exhibited a

187   significant decrease in cortisol levels over time, whereas the control group demonstrated an increase [65].

188   This animal support system can help ease the anxiety and stress experienced by children traumatized by serious

189   abuse. For example, studies have indicated that therapy dogs' presence during forensic interviews substantially

190   reduces physiological stress markers in sexually abused children. Specifically, children in the intervention group

191   who interacted with therapy dogs exhibited decreased systolic blood pressure (t (16) = −2.551, p = .021) and

192   diastolic blood pressure (t (16) = −3.019, p = .008) compared to those who did not. Heart rate prior to the forensic

193   interview was notably lower in the intervention group (M = 82.68, SD = 12.37) compared to the control group (M =

194   91.57, SD = 15.51; t (40) = 2.020, p = .050). While cortisol levels in the intervention group did not show significant

195   changes, the control group demonstrated a notable decrease in cortisol levels after the AAI interview (t (20) = 2.346,

196   p = .029). These findings suggest that therapy dogs provide consistent emotional and physiological support,

197   potentially alleviating the discomfort and stress of children during forensic interviews [66].

198   The development of stress-coping programs via CAI has shown its advantages in adults, such as college students.

199   Two studies have explored the effects of CAI on students' stress levels. In one study, self-reported stress scores and

200   vital signs were used to evaluate the stress levels of college students who were allowed to interact freely with a

201   therapy dog for 15 minutes during their final exams. Self-reported data showed significant reductions in stress levels,

202   with the PSS scores decreasing from 34.75 to 31.47 (mean difference = 3.28, SD = 3.22, p = .001). VAS measures

203   also revealed notable decreases, including stress (70.97 to 41.71, mean difference = 29.26, p = .001), sadness (34.49

204   to 12.29, mean difference = 22.20, p = .001), confusion (31.29 to 14.57, mean difference = 16.71, p = .001), and

205   anger (25.31 to 10.34, mean difference = 14.97, p = .001). Physiological assessments corroborated these findings,

206   indicating reductions in systolic blood pressure (131.09 mm Hg to 122.79 mm Hg, mean difference = 8.30 mm Hg,

207   p = .001) and pulse rate (80.68 bpm to 76.83 bpm, mean difference = 3.85 bpm, p = .039), although diastolic blood

208   pressure changes were not significant (81.72 mm Hg to 80.02 mm Hg, p = .104). Additionally, salivary cortisol

209   levels decreased significantly from 0.26 to 0.21 µg/dL (mean difference = 0.057, SD = 0.157, p < .015) [67]. This

210   result is supported by another study with a comparable methodology, which revealed that one-off meetings with

211   therapy dogs mediated the stress levels of students before final exams [68]. Specifically, the students interacted with

212   a therapy dog for 15 minutes in a single session and self-reported their stress scores. The stress scores of students

213   who interacted with the dog markedly declined with those in the control group.

214 For instance, in one study, students who participated in the therapy dog session reported a mean reduction of 3.6

215 points in their Stress VAS scores (SD = 2.35, p < .001, d = 1.57), indicating a large effect size. Conversely, students

216 in the control group experienced a slight increase in stress scores, with a mean increase of 1.2 points (SD = 2.89, d =

217 0.40), which reflected a medium effect size. These findings suggested that short-term CAI programs may be used as

218 an economical and easily accessible way to enhance the well-being of students [68].

219 Studies have explored the effects of CAI on children and young people and suggested that CAI effectively

220 reduces human stress. However, these studies are limited by the narrow age range of subjects and limitations of the

221 methods used to measure stress. Self-reporting surveys are among the most common methods for measuring stress,

222 but their reliability is limited due to subjectivity. Physiological indicators, such as cortisol [46, 69, 70] and heart

223 rates [71, 72], have been used to supplementary measures to validate the effects of CAI on stress levels. Nonetheless,

224 more diverse measures (e.g., various hormones like oxytocin or electroencephalography to more precisely validate

225 brain activities) can enhance the accuracy of stress measurement. Therefore, further studies should be performed to

226 diversify the age range of subjects and assess the effects of CAI by using various measurements to optimize its

227 effectiveness.

Depression in physiology

Depression is defined as a loss of pleasure in activities or a depressive mood that is more severe and lasts longer than a general emotional response [73]. It adversely impacts approximately 280 million people worldwide, or about 5% of adults [73]; consequently, this condition affects all aspects of life, including relationships with family, friends, and communities, and causes problems at school and work. The risk of depression is highest in adults aged over 60 years, with a prevalence rate of 5.7% [74]. Depressive disorders in seniors are characterized by diagnostic complexity, which is often accompanied by challenging clinical outcomes and a high risk of disability [75]. Therefore, developing the most effective treatments for patients suffering from depression is crucial.

Depression is associated with an imbalance of neurotransmitters and hormones. One of the major causes of depression is a decrease in neurotransmitters such as serotonin [76, 77]. Such biochemical changes are crucial for understanding the mechanisms of depression and developing therapeutic strategies. Therefore, understanding the underlying causes of depression is essential for creating effective therapeutic methods [78].

Serotonin is a neurotransmitter that regulates various physiological functions in the central and peripheral nervous systems [79]. It is primarily synthesized in the raphe nuclei in the brainstem and widely distributed throughout the neural network [80]. It participates in mood regulation, sleep, appetite, digestion, learning, memory, and other functions. It is also involved in emotion and mood stabilization [81, 82].

A serotonin imbalance is a major cause of depression. Decreased serotonin levels in the brain can result in depressive symptoms such as low mood, lethargy, and insomnia [77, 83]. These biochemical changes are crucial in understanding the mechanisms of depression and developing effective therapeutic strategies. Therefore, disturbances in the serotonin system are associated with mental disorders such as anxiety disorders and obsessive-compulsive disorders [83].

In the treatment of depression, selective serotonin reuptake inhibitors (SSRIs) inhibit the reuptake of serotonin in presynaptic neurons, thereby increasing serotonin levels. Through this mechanism, SSRIs enhance the efficacy of neurotransmission and alleviate depressive symptoms [84, 85]. This medical treatment is based on the neurobiological role of serotonin and has demonstrated effective therapeutic results in many patients.

Consequently, current studies focus on non-invasive treatments such as CAI as potential alternatives or complements to medication [86].

Measurement of depression levels

Depression levels can be evaluated using various physiological and psychological indicators [87]. These indicators can be accurately and objectively assessed using different methods, including ELISA for serotonin, fMRI, hematological analysis of the NLR, positron emission tomography (PET) scans, retinal imaging, EEG, and self-report measures. Each method assesses different aspects of depression.

ELISA is a precise analytical technique used to measure specific protein or hormone concentrations in biological samples quantitatively. Serotonin, a neurotransmitter closely associated with depression, can be measured in blood, saliva, or other biological samples. In studies on depression, serotonin levels are used to evaluate neurotransmitter imbalances and monitor the effects of treatment [77].

fMRI is a crucial tool for visualizing the functional changes in the brain in studies on depression. It is used to observe short-term and acute stress responses in stress measurements; in depression studies, fMRI is primarily used to examine functional changes in brain regions such as the prefrontal cortex, hippocampus, and amygdala [88, 89]. For example, patients with depression may exhibit a decreased activation of the prefrontal cortex and an overactivation of the amygdala [88, 90]. fMRI is used to assess structural changes, such as reduced volume of the hippocampus. In particular, it is utilized to analyze changes in connectivity between the default mode network (DMN) and the executive function network (EFN); it is also used to assess their association with overactivation or hypoactivation related to self-referential thinking [91]. Brain network connectivity is crucial in understanding the neurobiological mechanisms underlying depression. Changes in connectivity within the DMN and EFN are closely related to overactivation or hypoactivation related to self-referential processing, and these changes affect mood control and cognitive function in patients with depression [88, 89, 91]. Analyzing these connectivity changes, fMRI contributes to the diagnosis of depression, evaluates therapeutic effects, and aids in developing individualized therapy strategies [91].

Hematological analysis measures the NLR to evaluate changes in inflammation responses and immune function in depression studies. The NLR primarily indicates the inflammatory responses related to acute stress in stress assessments; in depression assessments, the NLR quantifies chronic inflammation. Chronic inflammation is closely associated with depression and can cause depressive symptoms by affecting neurotransmitter metabolism and neuroplasticity. A high NLR may be related to increased inflammatory cytokines, and the increase in inflammatory cytokines helps elucidate the pathophysiology of depression. The NLR can be compared before and after

283 antidepressant treatments to estimate the therapeutic effects and changes in inflammatory responses [92, 93].

284 PET scans are applied to elucidate the neurobiological mechanisms of the brain and evaluate the diagnosis and
285 therapeutic effects in depression studies [94]. They help reveal the complex characteristics of depression by
286 estimating the activation of neurotransmitter systems, brain metabolic activity, and changes in connectivity within
287 intracerebral networks. Specifically, they directly estimate the activation of neurotransmitter systems, such as
288 serotonin and dopamine [95, 96]. For example, the density of serotonin receptors or the activity of dopamine-related
289 targets can be analyzed to assess their association with depression. However, prudence is required in their clinical
290 application because of the high cost, radiation exposure, and time consumption associated with PET scans.

291 Retinal imaging is a non-invasive technique that captures accurate images of the retina, which is the light-
292 sensitive layer located behind the eye [97]. The retina shares the same embryonic origin as the brain; thus,
293 neurobiological changes associated with mental disorders can be indirectly observed by monitoring retinal changes
294 [98, 99]. Depression includes various neurobiological alterations, such as neuroinflammation, neurodegeneration,
295 and changes in neurotransmitter systems [100]. These changes manifest in the retina, reflecting similar processes
296 occurring in the brain [101]. For instance, the retina can undergo structural and functional changes because of
297 chronic inflammation and oxidative stress, which are commonly observed in depression [102]. Retinal imaging
298 techniques are mostly painless and do not require surgery [103]. Additionally, the detailed images of retinal
299 structures can be used as a basis for the early detection of diseases. However, these techniques are costly and require
300 expert interpretation.

301 The EEG is a non-invasive technique that records the electrical activities of the brain. It is used to identify
302 potential neural biomarkers and understand neurobiological mechanisms. It is a useful tool for understanding the
303 neurobiological characteristics of depression. However, there is a lack of consistency among studies. Increased delta
304 wave activity and alpha asymmetry may be associated with depression; however, relying solely on EEG as an
305 indicator lacks scientific robustness [99, 104]. Therefore, further studies should investigate EEG for evaluating
306 depression. Future research should involve larger sample sizes and apply EEG in conjunction with other biometric
307 indicators, such as hormone levels.

308 Self-report measures for depression include the Beck Depression Inventory (BDI), Hamilton depression rating
309 scale, and Geriatric Depression Scale (GDS) for the elderly. These questionnaires assess the severity and range of
310 symptoms associated with depression [105-107].

Effects of CAI on depression in elderly

As depression is recognized as a medical condition, studies on depression have focused on a limited range of subjects in specific situations. One study demonstrated that CAT alleviates depressive symptoms in elderly patients with psychosis, as assessed using the GDS. The findings revealed a significant reduction in GDS scores among participants in the pet group, decreasing from 5.9 ± 4.7 to 2.7 ± 3.1 ($p = .013$), indicating a marked improvement in depressive symptoms [108]. These findings suggest that CAT is effective in alleviating depression among older adults with psychosis. Another study has explored the effects of CAI on residents of long-term care facilities [14]. The treatment group interacted with a therapy dog once a week for 6 weeks. Depression was assessed using the BDI. The results indicated that the average self-report scores of the treatment group significantly improved, with BDI scores decreasing from 15.4 ± 4.2 to 10.7 ± 3.8 ($p = .017$), whereas the scores of the control group did not have significant changes [14]. Therefore, CAI may be beneficial to residents of long-term care facilities. This finding is supported by several studies that highlight the effects of CAI in reducing depressive symptoms in individuals with dementia [13]. They demonstrated that depression levels significantly decreased in participants with severe dementia after the CAI program. For instance, in one study, depression levels measured by the DMAS showed a mean decrease of 4.5 points from baseline ($p < .001$) in the CAI group, while the control group exhibited a significant increase of 4.9 points ($p < .001$) [13]. Thus, CAI positively affects depression in people with dementia, especially in later stages.

In addition, qualitative studies emphasize the significant role of dogs in enhancing the physical and psychological well-being of elderly individuals with chronic illnesses. Interactions with companion animals encourage physical activity, foster emotional bonding, and provide companionship, thereby contributing to the management of depressive symptoms. For example, engaging in caregiving activities such as walking or grooming pets not only increases physical activity but also boosts self-efficacy and fosters a sense of purpose. Moreover, companion animals act as sources of comfort and joy, helping to alleviate feelings of loneliness and isolation. In this respect, incorporating companion animals into therapeutic programs for the elderly can effectively alleviate depressive symptoms and improve overall quality of life [109].

Depressive symptoms often accompany chronic pain and a loss of interest in activities; these symptoms can exacerbate in terms of duration, pain intensity, and functional impairment [110], particularly in older adults. Dogs contribute to pain management by bringing joy and laughter [109]. Furthermore, activities involving therapy dogs,

339   such as brushing or walking them, can increase physical activity in patients; thus, their self-efficacy can be enhanced

340   by enabling them to provide meaningful care during older adulthood. For instance, a study reported that patients

341   who participated in therapy dog-related activities demonstrated a significant increase in daily physical activity levels,

342   walking an additional average of 1,500 steps per day compared to the baseline ($p < .05$). These findings suggest that

343   therapy dog interactions not only promote physical activity but also foster a sense of purpose and capability in older

344   adults [111].

345   The majority of studies have demonstrated that CAIs effectively alleviate depressive symptoms. As such, they

346   show potential for therapeutic applications in mental health care to manage depression. Additionally, implementing

347   CAIs in nursing homes or community spaces with seniors may be beneficial in the long term because it involves

348   participation in recreational activities that improve the physical, mental, and social well-being of older adults.

349   However, further studies should explore the long-term effects of CAIs, diversify the range of participants, and

350   investigate the specific mechanisms through which CAIs exert their therapeutic benefits for depression.

351   To maximize the therapeutic potential of CAIs, developing customized programs tailored to individuals' symptoms

352   and needs is essential. Such programs could enhance the effectiveness of CAIs in managing stress and depression,

353   particularly in diverse populations. As a result, generalizing the effects of CAIs across diverse situations is

354   challenging. Therefore, this review aims to establish optimized CAI programs for various subjects and maximize the

355   effects of CAI in managing depression and stress. To achieve this objective, this review integrates various biometric

356   indicators and physiological evaluation tools to analyze the effects of CAI through multiple approaches.

Conclusion

This review explores the effectiveness of CAI in managing stress and depression in humans. Various studies show that CAI provides substantial advantages, including emotional support, physical interaction, and social engagement, which enhance mental health outcomes across diverse age groups. Vulnerable populations, such as the elderly and individuals with psychiatric conditions, particularly benefit from CAI because of the unique therapeutic bond formed with therapy dogs. Despite these promising outcomes, CAI has several limitations, including lack of standardized protocols, limited long-term studies, and variability in program implementations. Additionally, the mechanisms through which CAI exerts its effects are not fully understood. As such, further research is needed to bridge these gaps. Future studies should elucidate the underlying mechanisms of CAI, expand the diversity of participant groups, and conduct longitudinal assessments to evaluate the sustained effect of CAI. Moreover, integrating CAI with other therapeutic modalities may enhance its benefits. Therefore, CAI offers relevant clinical advantages in the field of mental health, serving not only as an effective tool for alleviating the symptoms of depression and stress but also as an efficient technique to improve the overall quality of life of individuals experiencing these challenges. Integrating CAI into mainstream mental health care practices has the potential to enhance therapeutic outcomes and provide a holistic approach to mental well-being.

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647 **Table 1. Measurements of stress**

Measurements	Description
ELISA	Used to evaluate cortisol levels.
fMRI	Mainly used to study the physiological mechanisms of the brain involved in psychological stress.
Hematological analysis for NLR	Useful for evaluating physiological responses to stress because the NLR increases under high-stress conditions.
EEG	In stressful situations, beta waves have an increased activity, particularly high beta waves (20-30 Hz).
HRV	Under stress, the HRV decreases because of sympathetic nervous system activation.
Self-report	Perceived Stress Scale, Visual Analog Scale

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649   **Table 2. Measurements of depression**

Measurements	Description
ELISA	Used to evaluate serotonin levels.
fMRI	fMRI is utilized to analyze changes in connectivity between the default mode network (DMN) and the executive function network (EFN).
Hematological analysis for NLR	The NLR primarily indicates the inflammatory responses related to acute stress in stress assessments; in depression assessments, the NLR quantifies chronic inflammation.
EEG	Increased delta wave activity and alpha asymmetry may be associated with depression; however, relying solely on EEG as an indicator lacks scientific robustness.
PET	PET scans are applied to elucidate the neurobiological mechanisms of the brain and evaluate the diagnosis and therapeutic effects in depression studies.
Retinal imaging	Retinal imaging is a non-invasive technique that captures accurate images of the retina, which is the light-sensitive layer located behind the eye.
Self-report	Beck Depression Inventory, Hamilton depression rating scale, geriatric depression scale

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651   **Table 3. Effects of CAI on stress in non-elderly**

Target group (n)	Application of CAI	Measurement Methods and Results	References
Children (n=134)	Randomized controlled trials involving AAI aimed to reduce stress levels in general education children (n=90) and special education children (n=44) during school activities. Conducted AAI sessions twice a week for 20 minutes each over 4 weeks.	Salivary cortisol levels were measured in both general education children and special education children. For general education children, cortisol levels decreased significantly compared to the control group. Similarly, special education children also showed a significant reduction in cortisol levels during intervention sessions, highlighting the effectiveness of AAI in reducing stress for both groups.	10
Children in acute care settings (n=80)	Randomly assigned to the Dog-assisted intervention (DAI) group (n=44) or waitlist control group (n=36). Therapy dog visits were conducted for the DAI group. The CAI group received dog visits for 5-10 minutes while the control group did not.	Stress was measured via salivary cortisol samples. Activity levels were also recorded. The CAI group showed increased interaction with the therapy dog and reduced stress levels compared to the control.	66
Sexually abused children (n=42)	Children were assigned to an intervention group (AAI with therapy dog, n=19) or a control group (standard interview protocol, n=23). In the intervention group, children could pet and talk to the therapy dog during the forensic interview.	Cardiac assessments included blood pressure (BP), heart rates (HR), and saliva samples for cortisol and immunoglobulin A (IgA). The control group had significantly higher HR before the interview, indicating higher stress. Significant decreases in BP were observed in an intervention group. The intervention group showed lower HR and BP, indicating reduced physiological stress. No significant differences in cortisol or IgA were found.	67
College Students (n=48)	Interaction with therapy dogs for 15 minutes during final exams.	Stress levels were assessed using the Perceived Stress Scale(PSS), visual analog scales(VAS), vital signs, and salivary cortisol measurements before and after the intervention. Significant reductions were observed in all measures except diastolic blood pressure.	68
College Student (n=78)	Therapy dog intervention was conducted 1 week before final exams. Each session lasted for 15 minutes.	Stress was measured using the Perceived Stress Scale, Stress Visual Analog Scale (SVAS), saliva for nerve growth factor (sNGF), and alpha amylase (sAA). SVAS scores significantly decreased after intervention, indicating reduced perceived stress. No significant differences in physiological measures (sAA).	69

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653 **Table 4. Effects of CAI on depression in elderly**

Target group (n)	Application of CAI	Measurement Methods and Results	References
Elderly Inpatients (n=21)	6-week intervention in a nursing home, 90 minutes once a week for the pet group (n=10). Participants interacted with therapy dogs (holding, walking, talking, playing) under supervision. The control group (n=11) observed but did not interact.	Cognitive function was measured using a Mini-Mental State Examination (MMSE), and depression was measured using the Geriatric Depression Scale (GDS). GDS scores improved by 50% within the pet group, and MMSE scores increased. Quality of life was also reported to have improved.	109
Residents in long-term care (n=16)	AAA group (n=8) received 30-minute visitations once a week for 6 weeks. The control group (n=8) residents never saw the therapy dog until after the post-measures were done.	Depression and anxiety were measured using the Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) pre-and post-intervention. Significant reduction in depression (BDI) in the AAA group, and no significant changes in anxiety (BAI).	14
Nursing home residents with dementia (n=54)	Participants (n=54) were randomly assigned to the AAT group (n=27) and control group (n=27). AAT was conducted for 10 weeks (once a week, 45 minutes) in a nursing home after preparation with the therapy center. The control group received their usual pharmacologic and nonpharmacologic treatments without AAT.	Symptoms of agitation/aggression and depression were assessed using the Cohen-Mansfield Agitation Inventory and Dementia Mood Assessment Scale. The control group showed increased symptoms over 10 weeks. The intervention group maintained constant levels of symptoms.	13

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