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Comparison of the Effectiveness of Acceptance and Commitment Therapy and Emotion-Focused Therapy on the Burden of Caregivers of Individuals with Dementia

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A B S T R A C T

Objective: The present study aimed to compare the effectiveness of Acceptance and Commitment Therapy (ACT) and Emotion-Focused Therapy (EFT) on the burden of caregivers of individuals with dementia.

Methods and Materials: This research employed a quasi-experimental method with a pretest-posttest-follow-up design and a control group. The statistical population of this study was selected from the primary caregivers (wives and daughters) of individuals with dementia who visited the Iranian Dementia Association (located in Tehran) in 2023. From this population, 45 subjects were purposefully selected and randomly assigned to three equal groups of 15 (two experimental groups and one control group). To collect data, the Caregiver Burden Scale by Novak and Guest (1989) was utilized. Data were analyzed using SPSS software and multivariate analysis of covariance (MANCOVA) tests.

Findings: The results indicated that both ACT and EFT interventions had a significant effect on reducing the burden of caregivers of individuals with dementia in the post-test and follow-up phases compared to the control group.

Conclusion: The findings suggest that ACT had a greater impact on reducing the burden of caregivers of individuals with dementia compared to EFT.

Keywords: *Acceptance and Commitment Therapy, Emotion-Focused Therapy, Caregiver Burden, Dementia*

1. Introduction

Dementia syndrome refers to a collection of symptoms that affect an individual's memory, thinking, and social abilities, leading to disruptions in daily functioning (Woods et al., 2023). Other symptoms related to dementia include difficulties in thinking, problem-solving, and language and speech problems. These changes typically start as minor and mild but gradually become severe enough to impact the individual's daily life (Shi et al., 2023). The high costs of hospital care on one hand and individuals' preference for non-hospital living conditions on the other hand have led to an increasing demand for non-hospital care services today (Martin et al., 2023). The debilitating nature

of the disease necessitates many individuals with dementia to receive assistance through caregivers (Ramezani et al., 2023b). Following the diagnosis of dementia and the initiation of the treatment process, a sense of responsibility arises in the patient's family members to provide care. Consequently, taking on the caregiver role is often unpredictable and not a matter of choice, appearing somewhat unavoidable (Nichols et al., 2022). Thus, chronic illness not only creates problems for the afflicted individual but can also cause issues for other family members who take on caregiving roles (Fazeli et al., 2022). One of these issues is that caring for individuals with dementia is associated with increased caregiver burden, which leads to a decrease in quality of life and general health (Tzourio, 2007). Caregiver burden is defined as the physical, psychological, and social reactions of the caregiver that result from the imbalance between caregiving needs and other responsibilities. This imbalance pertains to social roles, personal status, physical conditions, emotional states, and financial resources of the caregiver (Capozza et al., 2023).

Due to the low prevalence of dementia in recent years, researchers have paid special attention to two therapeutic strategies: Acceptance and Commitment Therapy (ACT) and Emotion-Focused Therapy (EFT). One proposed treatment for the problems faced by caregivers of patients is ACT. Instead of changing cognitions, this therapy aims to increase the psychological connection between the individual and their thoughts and feelings. ACT is a psychological intervention that is reinforced by cognitive defusion and experiential avoidance (Barnes et al., 2023). ACT includes six central processes that lead to psychological flexibility: acceptance, defusion, self-as-context, contact with the present moment, values, and committed action. The major advantage of this method compared to other psychotherapies is its focus on motivational aspects along with cognitive aspects for more effective and sustained treatment impact (Karimirad et al., 2018). Recent research on ACT has provided satisfactory results and rational reasons for using ACT in clinical practice, especially with patients suffering from mood and anxiety disorders. Another intervention that has garnered attention from psychologists in recent years is EFT. EFT is an integrated approach combining systematic, humanistic, and attachment theory perspectives. Given the major role of emotions in attachment theory, this therapy highlights the significant role of emotions and emotional connections in organizing communication patterns, considering emotions as the fundamental agent of change, and aims to identify feelings and transform them into comprehensible messages and constructive behaviors (Conroy et al., 2023). EFT involves methods based on activating strong primary emotions in an empathic communicative context (Del Bianco et al., 2023). Studies indicate that EFT is effective on quality of life, pain experience, and mood in patients with colorectal cancer and stress in individuals with chronic pain (Denton et al., 2012). Given the various therapeutic strategies available for addressing the problems of caregivers of patients with dementia, the researcher intends to investigate and study the effects of two therapeutic approaches, ACT and EFT, on the variables related to the burden of caregivers of individuals with dementia.

2. Methods and Materials

2.1. Study Design and Participants

The present study is an applied research type and, in terms of research method, is quasi-experimental with a pretest-posttest-follow-up design and a control group. The statistical population of the research included primary caregivers (wives and daughters) of individuals with dementia who visited the Iranian Dementia Association (located in Tehran) in 2023. In this study, a convenience sampling method was used. Primary caregivers of elderly dementia patients were requested to respond to the Caregiver Burden Inventory (CBI) while ensuring confidentiality, voluntary participation, absence of illness history, and non-receipt of treatment (medication and psychotherapy). After initial screening, 45 individuals were selected. Since it is recommended that group sizes in psychotherapy should not exceed 10 to 15 individuals (Sanaei, 2005), the number of group members in this study is considered appropriate. Given the sample adequacy of 15 subjects per group, 45 caregivers of individuals with dementia were selected based on the research entry criteria and willingness to participate in the study. They were non-randomly purposively selected and randomly assigned to two experimental groups of 15 and one control group of 15. The first experimental group received ACT, the second experimental group received EFT, and the control group received no treatment. Post-tests were administered, and follow-up tests were conducted three months later.

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2.2. Measures

2.2.1. Caregiving Burden

This standardized questionnaire consists of 24 questions and five dimensions of caregiver burden: time-dependent burden, developmental burden, physical burden, social burden, and emotional burden, based on a five-point Likert scale. The Caregiver Burden Inventory (CBI) is designed to assess the caregiving burden across five dimensions: time-dependent burden, developmental burden, physical burden, social burden, and emotional burden. In Novak and Guest's study, the reliability and validity of this questionnaire were measured. Responses are on a five-point Likert scale ranging from 1 (completely false) to 5 (completely true). Scores range from 24 to 120, with scores from 24 to 39 indicating mild burden, 40 to 71 indicating moderate burden, and 72 to 120 indicating severe burden (Abbasi et al., 2013). The question numbers for the dimensions are as follows: time-dependent burden: questions 1 to 5; developmental burden: questions 6 to 10; physical burden: questions 11 to 14; social burden: questions 15 to 19; emotional burden: questions 20 to 24. In the standard Caregiver Burden Inventory by Novak and Guest (1989), the reliability for time-dependent and developmental burden was found to be 0.85. The Cronbach's alpha for the physical burden, social burden, and emotional burden subscales were 0.86, 0.73, and 0.77, respectively. The validity of the Caregiver Burden Inventory was confirmed through content and face validity in Abbasi et al.'s (2013) study, and reliability was reported with Cronbach's alpha ranging from 69% to 87%, with the overall questionnaire's Cronbach's alpha being 80%. In Haqgoo et al.'s (2017) study, the validity and reliability of this questionnaire were confirmed. Shafi Zadeh et al. (2019) examined the validity and reliability of the Persian version of the Caregiver Burden Inventory in 150 caregivers of dementia patients. The total internal consistency for the subscales was 0.93. The test-retest reliability coefficient for the intra-class correlation index over a two-week interval was 0.96 (Ramezani et al., 2023a). In the present study, the validity and reliability of this tool were reassessed. The validity of the instrument was confirmed using face and content validity, and its reliability was found to be 0.86 using Cronbach's alpha.

2.3. Intervention

2.3.1. Acceptance and Commitment Therapy

The ACT protocol consists of ten sessions designed to help individuals develop psychological flexibility through acceptance, mindfulness, and committed action. Each session builds on the previous ones, introducing new concepts and techniques to aid participants in managing anxiety and stress by fostering a healthier relationship with their thoughts and emotions (Akbari Zargar et al., 2021; Azandariani et al., 2022; Barnes et al., 2023; Esmi et al., 2019; Fathi et al., 2021; Hadi Toroghi & Masoudi, 2020; Khademi & Tasbihsazan Mashad, 2019; Khalatbari et al., 2020; Mehryar, 2020; Shirazipour, 2022).

Session 1: Introduction

In the first session, group members are introduced to the therapist and each other. The purpose and structure of the therapy sessions are explained, along with the principles of ACT. Group rules are established, and participants share their views and experiences related to anxiety and stress in daily life.

Session 2: Creative Hopelessness

This session focuses on developing insight into the participants' control and avoidance strategies regarding anxiety. The ineffectiveness of these strategies is highlighted, encouraging acceptance of painful events instead of struggling against them.

Session 3: Acceptance

Participants are introduced to the concept of acceptance as an alternative to control and avoidance. The distinction between tolerance and acceptance is clarified. Techniques such as willingness to experience negative emotions and the "Healing Hands" exercise are practiced.

Session 4: Cognitive Defusion

The session covers the concepts of cognitive fusion and defusion. Participants explore their experiences of avoidance and fusion and practice observing their thoughts without judgment.

Session 5: Mindfulness and Present Moment Awareness

Mindfulness techniques are introduced and practiced, emphasizing staying connected to the present moment. The idea of self as context is also discussed.

Session 6: Values Identification

Participants identify and define their core values, differentiating between goals and values. They identify barriers to living in accordance with their values and engage in exercises related to satisfaction and dissatisfaction with life's struggles.

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Session 7: Committed Action

Goals are set based on identified values. The concept of committed action is defined, and participants plan specific actions to pursue their goals and values.

Session 8: Activity and Focus

The session discusses stages of activity and the activity cycle, giving participants concentration exercises and continuing the discussion on deriving satisfaction from life's challenges.

Session 9: Exposure and Empowerment

Exposure exercises are conducted while walking, and further exercises on clarifying values are included. The session emphasizes empowering participants to take control of their lives.

Session 10: Motivation and Committed Action

Participants are encouraged to engage in committed action with acceptance of mental experiences. The session aims to instill motivation and a proactive approach towards life goals.

2.3.2. Emotion-Focused Therapy

The EFT protocol consists of ten sessions that integrate systematic, humanistic, and attachment theories to address emotional experiences. The therapy focuses on identifying, expressing, and regulating emotions, facilitating emotional processing and transformation (Akbari Zargar et al., 2021; Conroy et al., 2023; Denton et al., 2012; Ebrahimi et al., 2022; Fathi et al., 2021; Greenberg et al., 2010; Sanagavi Moharrar et al., 2019).

Session 1: Establishing Therapeutic Relationship

A therapeutic relationship based on empathy and emotional feedback is established. Participants' expectations and concerns are assessed, and they are educated about the therapy. Emotional education brochures and emotion logs are distributed.

Session 2: Awareness and Identification of Emotions

Participants begin by discussing their current problems and identifying painful emotional experiences. Emotional awareness is initiated, and emotion logs are utilized to recognize emotionally intelligent thoughts.

Session 3: Emotional Processing

Participants engage in emotional processing through awareness, acceptance, tolerance, and regulation. The session involves accompanying and observing participants' emotional styles.

Session 4: Uncovering Core Emotions

Core and instrumental emotions are explored through techniques like working with an empty chair. Participants are guided to uncover their primary emotions.

Session 5: Continued Emotional Exploration

Further identification, representation, and regulation of underlying adaptive and maladaptive emotions continue. The session builds on previous work.

Session 6: Addressing Emotional Blockages

Participants identify and work on blockages to accessing primary and secondary emotions. Potential themes and images related to object representations are traced.

Session 7: Expressive Arts Techniques

Remaining emotional markers are addressed using expressive arts such as bodywork, music, and movements to facilitate deeper emotional expression.

Session 8: Gaining Insight

Participants achieve insight during the representation of objects. The session focuses on creating new understandings of their emotional experiences.

Session 9: Evaluating New Meanings

The session evaluates how new meanings formed through emotional processing contribute to the development of a new self.

Session 10: Consolidating the New Self

Participants work on stabilizing their new self-concept and applying it to future scenarios, ensuring the generalization of therapeutic gains.

2.4. Data analysis

Descriptive statistics (frequency, percentage, mean, and standard deviation) and inferential statistics (covariance analysis, Shapiro-Wilk test, Levene's test, M-Box test for covariance matrices in multivariate state) were used for data analysis. Univariate and multivariate covariance analysis was used to test the research hypothesis, and the eta coefficient was calculated to determine the effect size. Bonferroni's post hoc test was used to reveal differences between the groups. The above tests were performed using SPSS software version 27.

3. Findings and Results

Descriptive statistics related to the research variables, namely the caregiver burden of participants in the study, are presented in Table 1.

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Table 1

Means and Standard Deviations of Caregiver Burden in the Study Sample

Variable	Group	Mean Pre-test	Mean Post-test	Mean Follow-up	SD Pre-test	SD Post-test	SD Follow-up
Caregiver Burden	Control	85.25	85.10	85.15	15.14	14.85	15.08
	Experimental (ACT)	85.35	63.60	66.40	15.18	11.96	12.05
	Experimental (EFT)	85.10	72.30	76.45	15.14	13.06	13.16

Before inferential analysis, the main assumptions of multivariate covariance analysis were examined: 1) normality of score distribution, 2) homogeneity of variances, 3) equality (homogeneity) of variance-covariance matrices, and 4) homogeneity of regression slopes.

The Kolmogorov-Smirnov test was used to examine the assumption of normality of score distribution. The null hypothesis of normal distribution of scores in the pre-test, post-test, and follow-up stages for the three groups was not rejected, confirming the normality assumption for the scores in all groups ($p \geq 0.05$).

Levene's test was employed to check the assumption of homogeneity of variances. The assumption of equal variances was confirmed for all research variables in the post-test and follow-up stages ($p \geq 0.05$).

To test the assumption of equal covariances or relationships among dependent variables, the M Box test was used. The results indicated that the condition of homogeneity of variance-covariance matrices was met (M box = 124.63, F = 1.23, p = 0.06).

The interaction F between the pre-test and group for each dependent variable was calculated to examine the homogeneity of regression slopes. The results showed that the interaction between group and pre-test was not significant for any dependent variables ($p \geq 0.05$), indicating that the assumption of homogeneity of regression slopes was met for all research variables.

Table 2

Univariate Covariance Analysis Results for Post-test and Follow-up Caregiver Burden

Research Stage	Source	Variable	Sum of Squares	df	Mean Square	F	p	Eta
Post-test	Group Membership	Caregiver Burden	2374.83	2	1187.41	182.59	0.001	0.85
Follow-up		Caregiver Burden	1443.005	2	721.40	80.73	0.001	0.83

According to the results in Table 2, after removing the effect of pre-test scores, the difference in post-test mean scores for caregiver burden among the two experimental groups (ACT and EFT) and the control group was significant ($p \leq 0.001$). The results indicate that the adjusted mean differences in post-test caregiver burden scores by group were significant ($p \leq 0.001$), with an 85% impact on reducing caregiver burden at the post-test stage. Similarly, the difference in follow-up mean scores for caregiver burden among the groups was significant ($p \leq 0.001$), with an 83% impact on reducing caregiver burden at the follow-up stage. To further investigate the differences between the experimental and control groups in terms of caregiver burden at the post-test and follow-up stages, Bonferroni pairwise comparisons were conducted on the adjusted means, as reported in Table 3.

Table 3

Bonferroni Test Results for Adjusted Mean Differences by Group

Research Stage	Variable	Group	Comparison Group	Mean Difference	p
Post-test	Caregiver Burden	Control	ACT	21.50	0.001
			EFT	12.80	0.001
		ACT	Control	-21.50	0.001
			EFT	-8.70	0.001
		EFT	Control	-12.80	0.001
			ACT	8.70	0.001
Follow-up	Caregiver Burden	Control	ACT	18.75	0.001
			EFT	8.70	0.001

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ACT	Control	-18.75	0.001
	EFT	-10.05	0.001
EFT	Control	-8.70	0.001
	ACT	10.05	0.001

The results in Table 3 indicate that both ACT and EFT interventions resulted in significant differences in caregiver burden compared to the control group at both post-test and follow-up stages ($p \leq 0.001$). Furthermore, the results demonstrate that ACT had a greater impact on reducing caregiver burden among female and daughter caregivers of individuals with dementia compared to EFT, with a reduction of 8.70 points at the post-test stage and 10.05 points at the follow-up stage.

4. Discussion and Conclusion

The aim of this study was to compare the effectiveness of Acceptance and Commitment Therapy (ACT) and Emotion-Focused Therapy (EFT) on the burden of caregivers of individuals with dementia. The results showed that both ACT and EFT interventions significantly reduced caregiver burden compared to the control group at both post-test and follow-up stages. Additionally, the results indicated that ACT had a greater impact on reducing caregiver burden among female and daughter caregivers of individuals with dementia compared to EFT, with reductions of 8.70 points at the post-test stage and 10.05 points at the follow-up stage.

Due to the novelty of this research and the lack of similar studies, the results cannot be directly compared to other studies. However, the findings of this study align with parts of the results from the prior studies (Akbari Zargar et al., 2021; Azandariani et al., 2022; Barnes et al., 2023; Conroy et al., 2023; Denton et al., 2012; Ebrahimi et al., 2022; Esmi et al., 2019; Fathi et al., 2021; Greenberg et al., 2010; Hadi Toroghi & Masoudi, 2020; Khademi & Tasbihsazan Mashad, 2019; Khalatbari et al., 2020; Mehryar, 2020; Sanagavi Moharrar et al., 2019; Shirazipour, 2022).

In explaining the effectiveness of ACT on the burden of caregivers of individuals with dementia, it can be stated that caregivers of individuals with dementia are exposed to stressful factors and face various challenges, leading to significant changes in their adaptability (Barnes et al., 2023; Khalatbari et al., 2020). Some caregivers adapt to these challenges, while others feel unsupported and add to their problems, increasing their caregiver burden. ACT helps these individuals to let go of the problem and experience it in a manner compatible with life. This approach strengthens present-moment awareness, helping caregivers live in the present and accept the problem instead of denying and engaging in problematic thoughts, thereby experiencing fewer caregiver burdens (Akbari Zargar et al., 2021).

Furthermore, defusion exercises help individuals respond more adaptively and flexibly to their inner experiences instead of becoming entangled with their current thoughts. Additionally, practicing values and committing to them encourages behavior that is reinforcing in the long term rather than short-term experiential avoidance. Consequently, specifying clear and actionable behaviors helps caregivers manage mental barriers and caregiver burdens during challenging situations (Barnes et al., 2023; Esmi et al., 2019).

Caring for individuals with dementia is associated with caregiver anxiety, stress, and depression, reducing their quality of life and general health. Dementia causes significant negative emotional burdens for caregivers, affecting their motivation and psychological state. Another explanation for the greater effectiveness of ACT is that it helps participants experience their troubling thoughts and feelings as mere thoughts and move toward their values rather than responding to them. ACT aims to increase acceptance of mental experiences and reduce ineffective avoidance behaviors. Caregivers are taught that avoidance or suppression of these unwanted mental experiences is ineffective and often counterproductive, exacerbating them. Instead, they are encouraged to fully accept these experiences without internal or external reactions aimed at eliminating them.

In subsequent stages, individual awareness of the present moment is increased, and caregivers learn to separate themselves from these mental experiences (cognitive defusion), allowing them to act independently of these experiences (Mehryar, 2020). The next step involves reducing excessive focus on self-concept or personal narratives (e.g., victimhood). Finally, caregivers are helped to identify and clarify their core personal values and convert them into specific behavioral goals (value clarification). This process, called creating motivation, leads to committed actions towards the specified values, accompanied by acceptance of mental experiences, resulting in reduced negative emotions like caregiver burden.

During the intervention, participants learned to enjoy life and find satisfaction despite problems and the non-

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responsiveness of thoughts, bodily symptoms, memories, and urges. They learned to move towards their values despite these challenges, reducing caregiver burden. The study also found that EFT was effective in reducing caregiver burden among individuals caring for dementia patients (Fathi et al., 2021; Greenberg et al., 2010).

The psychological, physical, and social stresses of long-term caregiving can lead to caregiver burden, resulting in problems such as burnout, anxiety, and depression for caregivers (Azandariani et al., 2022). Studies indicate that factors such as the caregiver's gender and the physical activity level of the elderly significantly impact caregiver burden. There is also a positive correlation between anxiety, depression, and caregiver burden. According to Fredrickson's (2004) broaden-and-build theory of positive emotions, creating and developing positive emotions can negate the effects of negative emotions and burdens. Through emotional processing during therapy sessions, the negative emotional burden was reduced (Capozza et al., 2023; Ramezani et al., 2023b).

EFT in this study seemed to include two aspects: the emphasis on the therapeutic relationship, which needs to be continuously received from the client, and the validation caregivers received for all their emotions and feelings. This led to rapid emotional experiences and extensive discussions during sessions (Ebrahimi et al., 2022). This can be explained by the integration of "being" and "doing" by the EFT therapist. The therapist follows the client's internal experience, which constantly changes, maintaining an empathic connection with the client's experience and understanding it, which can reduce caregiver burden.

Another explanation is that the emotion-focused approach emphasizes individual growth and reducing security-seeking conflicts in interpersonal relationships. Overall, EFT focuses on the participation of emotions in persistent maladaptive patterns among caregivers. The therapy aims to reveal vulnerable emotions and facilitate caregivers' ability to express them safely. It is believed that processing these emotions in a safe context creates healthier and new interaction patterns, improving the caregiver burden for individuals with dementia (Ardestani Balaie et al., 2021). Caregivers, with the help of a psychologist, identify their negative and vulnerable emotions and learn that using positive emotions can lead to psychological relief. They identify negative emotions and work to reduce them. According to this theory, emotions arise when internal and external inputs are processed to activate an emotional program (e.g., sadness and happiness). This triggers physiological changes (subjective feelings and behavioral impulses) preparing the individual to respond adaptively to environmental challenges or opportunities. Emotions suggest actions without dictating them, explaining why feelings are not always transparent. Emotional response tendencies can be expressed or remain unexpressed (Heydarian et al., 2020).

Caregivers with irregular cognitive processes impacting caregiver burden and increasing cognitive failures, along with behavioral outcomes, can lead to significant problems that are time-consuming to rectify. Through EFT training, caregivers can reduce their psychological burden and problems by increasing positive emotions. This approach can help caregivers enhance their interpersonal relationships and control them, experiencing less caregiver burden.

In explaining the greater effectiveness of ACT compared to EFT on caregiver burden among female and daughter caregivers of individuals with dementia, it can be stated that these caregivers often have to change family living conditions and some roles and responsibilities. They are psychologically influenced by the elderly's condition, and in addition to their economic and occupational responsibilities, they also bear the burden of caring for individuals with dementia. This relative superiority of ACT might be due to its focus on thoughts and cognitive schemas as a third-wave behavioral therapy. Techniques related to increasing defusion and acceptance help caregivers accept thoughts and feelings related to life and accompany them, focusing on strengths to take valuable actions during challenging situations caused by the illness.

The goal is to help individuals experience thoughts arising from schemas as mere thoughts and pursue what is important to them in life and aligns with their values. Meanwhile, although EFT has been effective in reducing caregiver burden, it focuses directly on emotions and their expression, which is the key concept in this approach. Given the cultural context in Iran, which tends to suppress negative emotions like anger, sadness, and fear, leading to socially acceptable secondary emotions, individuals face severe conflicts and confusion when confronting these emotions and focusing on them. This therapy approach requires more time and longer treatment periods to achieve its goals and establish safe relationships and new interactions.

ACT's greater effectiveness compared to EFT can be explained by the theory that a significant factor in creating and maintaining psychological burden and distress is experiential avoidance, which refers to the exaggerated negative evaluation of internal experiences like thoughts,

feelings, and emotions and the unwillingness to experience them, leading to efforts to control or escape them, potentially interfering with functioning. Caregivers with higher experiential avoidance experience fewer positive emotions and life satisfaction and feel their lives are meaningless (Esmi et al., 2019).

However, the goal of ACT is to reduce experiential avoidance and increase psychological flexibility by accepting unavoidable and distressing feelings like anxiety, cultivating mindfulness to neutralize over-involvement with cognitions, and identifying personal values related to behavioral goals. Caregivers are encouraged to engage fully with experiences without resistance and accept them without judgment regarding their correctness or incorrectness upon occurrence. This can explain ACT's greater effectiveness compared to EFT.

5. Limitations & Suggestions

One major limitation of this study is the convenience sampling method, which might affect the generalizability of the results and external validity. Based on the results, it is recommended that counselors use these two effective and practical therapeutic approaches in educational classes to reduce problems for caregivers of chronic patients.

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Declaration of Interest

The authors of this article declared no conflict of interest.

Ethical Considerations

The study protocol adhered to the principles outlined in the Helsinki Declaration, which provides guidelines for ethical research involving human participants.

Transparency of Data

In accordance with the principles of transparency and open research, we declare that all data and materials used in this study are available upon request.

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Authors' Contributions

All authors equally contributed in this article.

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