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Article

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Abstract: Recent advancements in technology have introduced novel therapeutic interventions for Alzheimer's Disease (AD). This study evaluates the feasibility of a Virtual Reality (VR) intervention for patients with mild to moderate cognitive decline, aiming to improve mood, evoke autobiographical memories, and enhance overall well-being. The intervention leverages personalized and emotionally evocative VR sessions paired with culturally and aesthetically tailored music. Seven elderly participants (6 with mild cognitive declining and 1 with moderate cognitive decline) were exposed to immersive 360-degree videos depicting familiar and non-familiar scenarios. Results demonstrated high levels of immersion and positive emotional responses, with notable memory recall linked to the multi-sensory stimuli. Despite minor side effects, such as fatigue or anxiety, participants generally found the experience engaging and meaningful. This feasibility study lays the groundwork for future large-scale trials and underscores the potential of VR as a complementary tool in cognitive rehabilitation strategies for AD.

Keywords: virtual reality; Alzheimer's disease; mild cognitive impairment; cognitive rehabilitation; music therapy; autobiographical memory; multisensory stimulation; feasibility study

1. Introduction

Alzheimer's Disease (AD) is a progressive neurodegenerative condition characterized by significant cognitive decline, emotional disturbances, and impaired social interactions. As one of the leading causes of disability in older adults, AD presents substantial challenges for patients, caregivers, and healthcare systems worldwide [1]. Early interventions that address behavioral symptoms and enhance quality of life are crucial for mitigating its impact.

For planning early interventions, it is crucial to identify the prodromal stages of Alzheimer's Disease (AD). Mild Cognitive Impairment (MCI), a condition associated with an elevated risk of progressing to AD, shows an estimated annual conversion rate of 10–15% in clinical settings, while community-based studies report lower rates, ranging from 3.8% to 6.3% annually. Long-term studies indicate that approximately 80% of individuals with MCI progress to AD over a six-year follow-up period [2,3]. MCI, often considered a prodromal stage of AD, is characterized by measurable deficits in cognitive functions—especially memory—that exceed normal aging expectations but do not significantly impair daily activities [4]. However, MCI represents a critical therapeutic window for interventions aimed at slowing cognitive decline and enhancing psychosocial well-being. Recent progress in Alzheimer's Disease (AD) research has led to a paradigm shift, viewing the disease not as a series of distinct stages but as a continuous process of neurodegeneration. This continuum framework captures the progressive and multifaceted nature of AD, beginning with asymptomatic

phases, progressing through Mild Cognitive Impairment (MCI), and culminating in full-blown dementia [5]. Figure 1 illustrates the escalating severity associated with each stage of the AD continuum.

However, this approach poses challenges in precisely pinpointing an individual's position within the continuum and assessing their specific risk factors for progression [6,7]. Accurate staging is critical for implementing early, targeted interventions that can delay or prevent irreversible neuronal damage and cognitive decline. This highlights the need for advanced diagnostic tools capable of identifying AD pathology in its earliest stages to maximize the potential benefits of therapeutic strategies.

Current therapeutic strategies for AD and MCI primarily involve pharmacological approaches, such as acetylcholinesterase inhibitors (donepezil, rivastigmine, galantamine) and NMDA receptor antagonists (memantine), which manage symptoms rather than halt disease progression [8]. Recently, Lecanemab, a monoclonal antibody targeting amyloid-beta aggregates, received FDA approval in July 2023, marking a milestone as one of the first treatments to target Alzheimer's pathology [9]. Lecanemab binds to soluble amyloid-beta protofibrils, facilitating clearance and slowing cognitive decline in early AD. In the Clarity AD phase 3 trial, it significantly reduced clinical decline over 18 months, improving cognitive and functional measures [10]. However, risks such as amyloid-related imaging abnormalities (ARIA) highlight the need for careful patient monitoring. While approved in the US, Lecanemab is not yet available in Italy, with EMA approval pending [11].
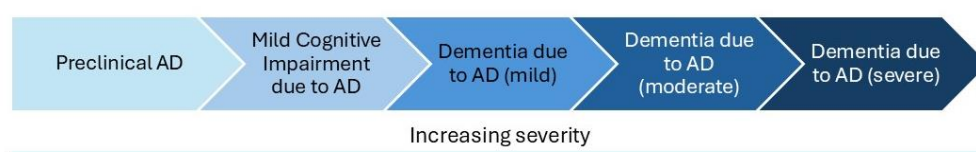

Figure 1. The Alzheimer's continuum, showing the progression from preclinical stages to severe dementia, with increasing severity of cognitive and functional decline across distinct stages of the disease. Modified from Parnetti, Chipi, Salvadori, D'Andrea, & Eusebi [6].

In turn, non-pharmacological therapies, including cognitive stimulation, physical activity, and diet modifications, have shown potential in slowing cognitive decline and improving overall well-being [12]. Complementary therapies, such as music therapy, art therapy, and mindfulness-based interventions, are gaining recognition for their ability to address behavioral symptoms, reduce anxiety, and enhance quality of life in both MCI and AD populations [13]. For instance, a meta-analysis of 15 studies investigating the effects of music therapy on Alzheimer's Disease (AD) patients reported significant improvements in cognitive abilities and daily living activities [14]. Another systematic review and meta-analysis found that non-pharmacological therapies, including music therapy, positively impacted activities of daily living (ADL), behavioral and psychological symptoms of dementia (BPSD), cognition, and quality of life (QoL) in individuals with moderate-to-severe dementia [15]. Furthermore, music therapy alone was shown to significantly enhance cognitive function and quality of life in patients with AD, as highlighted in a separate meta-analysis [16]. These findings underscore the importance of incorporating evidence-based non-pharmacological interventions, such as music therapy, into treatment plans. By integrating pharmacological and non-pharmacological approaches, a multimodal strategy can optimize patient outcomes, addressing both cognitive and emotional challenges associated with AD.

Additionally, emerging technologies, such as Virtual Reality (VR), offer promising opportunities in the therapeutic management of both MCI and AD. VR provides immersive environments that can engage cognitive and emotional processes, potentially improving mood, reducing anxiety, and stimulating autobiographical memory recall [17]. These attributes make VR particularly suitable for

addressing the challenges associated with cognitive decline in both MCI and early AD populations [18]. Recent systematic reviews and meta-analyses provide   evidence supporting the efficacy of VR interventions in this context. For example, Kim et al. [19] highlighted the positive impact of VR in MCI on cognitive function, daily living activities, and neuropsychiatric symptoms, underscoring its potential as a cognitive rehabilitation tool. Furthermore, Zhu et al. [20] investigated in individuals with MCI the effects of dual-task interventions combining motor and VR-based cognitive training, reporting enhanced executive function and gait performance. In these interventions, VR was primarily used to recreate both artificial and natural landscapes, including tasks designed to simulate real-world environments and activities.

Very recently, Yang et al. [21] conducted a meta-analysis of 18 randomized controlled trials conducted with VR interventions on MCI patients (722 participants were included), demonstrating significant improvements in cognitive functions among older adults with MCI compared to control groups. The effect sizes reported included a Standardized Mean Difference (SMD) of 0.20 (95% CI: 0.02–0.38) for memory, 0.25 (95% CI: 0.06–0.45) for attention and information processing speed, and 0.22 (95% CI: 0.02–0.42) for executive functions, indicating small to moderate improvements in these cognitive domains. Many of these scenarios included soundscapes, such as ambient environmental sounds like birdsong or flowing water, or music tailored to enhance relaxation and engagement. Additionally, VR has been used for dual-task exercises that combine cognitive challenges with motor activities, such as navigating virtual pathways or interacting with objects within the virtual space [17,19]. These findings emphasize the potential of VR as a therapeutic tool for mitigating cognitive decline and improving quality of life in individuals with MCI and early AD. At the same time, the scarcity of applications of VR for early AD compared to MCI, as well as the high costs of devices and the need for multiple sessions, highlight significant challenges to its accessibility and feasibility for long-term AD treatment. This underscores the need for implementing novel methodologies that are both cost- and time-effective, paving the way for more sustainable and widely applicable interventions.

Here, we build on previous studies with VR to evaluate the feasibility, accessibility and acceptability of a VR-based intervention with novel aesthetic and mnestic features for individuals with MCI and mild to moderate AD. By utilizing personalized, emotionally evocative and aesthetically appealing 360-degree videos and music, the intervention aims to improve mood, evoke autobiographical memories, and enhance overall well-being. The audio-video VR stimulation is rooted in research demonstrating the significant role of multi-sensory experiences in enhancing cognitive and emotional outcomes in aging populations [22]. Positive aesthetic experiences, such as engaging with visually and aurally pleasing stimuli, have been shown to promote emotional well-being, reduce stress, and foster a sense of tranquility [23–27]. Music, in particular, has a unique ability to evoke autobiographical memories, even in individuals with significant cognitive impairments, by stimulating neural pathways associated with memory and emotion [28,29].

The rationale for this specific VR intervention builds upon previous music-neuroaesthetic findings, leveraging the synergistic effects of immersive environments and evocative music to stimulate cognitive processes and elicit positive emotional responses. By integrating familiar landscapes and culturally relevant music, the intervention seeks to evoke memories, enhance mood, and provide a calming and meaningful experience tailored to the needs of individuals with AD or MCI.

2. Materials and Methods

- **Participants**

The study involved 7 elderly participants (2 males and 5 females) with a mean age of 70.44 ± 2.24 years (range: 68.5–75.25). All participants exhibited cognitive impairments compatible with an Alzheimer's Disease (AD) profile, as assessed by their MoCA scores. Specifically, six participants presented with mild cognitive impairments (MoCA scores: 18–25), while one participant exhibited moderate cognitive impairment (MoCA score: 10–17) [30]. These classifications align with the

Alzheimer's continuum framework, which describes a progression of cognitive decline consistent with AD-related pathology [5]. The mean MoCA score was 21.57 ± 2.48 (range: 17–24). Cognitive reserve, assessed via the Cognitive Reserve Index Questionnaire (CRIq), averaged 88.29 ± 11.94 (range: 76–109). Male participants had higher cognitive reserve scores (mean: 104 ± 7.07) than females (mean: 82 ± 6.97), reflecting established gender-related differences in cognitive reserve. Individual clinical and neuropsychological profiles are detailed in Table 1.

Participants were recruited through the Centro Servizi per le Famiglie "Libertà" di Bari. All participants or their caregivers provided informed consent after being briefed on the study's purpose and procedures.

All experimental procedures complied with the Declaration of Helsinki – Ethical Principles for Medical Research and were approved by the Ethics Committee at the For.Psi.Com Department of the University of Bari (ET-24-18-R1).

Table 1. - Demographic, clinical, and neuropsychological characteristics of the study participants. The table includes participant gender, age at the time of diagnosis (DEG.age), cognitive performance scores measured using the Montreal Cognitive Assessment (MoCA), and cognitive reserve levels assessed using the Cognitive Reserve Index Questionnaire (CRIq).

Participant	Gender	DEG.age	MoCa	Criq
1	Male	68.5	24	109
2	Male	75.25	22	99
3	Female	70	21	78
4	Female	71.25	21	87
5	Female	71.25	17	80
6	Female	70.08	24	89
7	Female	68.75	21	76

- **Neuropsychological and behavioral examination**

Self-assessments of mood are recorded before and after each video presentation through simple questions, and responses were noted each time. Following each video session, participants completed a custom-made questionnaire designed to assess their experience. The questionnaire included items from the Slater-Usoh-Steed (SUS) presence scale [31], the Visual Analogue Scale (VAS) [32] for mood evaluation and additional semi-structured questions developed by the research team to explore specific aspects of satisfaction with the VR experience, transient mood state, and any memory recollection triggered by the videos.

Eligibility of the participants is determined using MoCA (Montreal Cognitive Assessment), a brief cognitive screening tool with high sensitivity and specificity for detecting MCI [33].

The Cognitive Research Index Questionnaire (CRIq)[34] was administered to evaluate participants' cognitive reserve, accounting for their educational, occupational, and leisure activities throughout life.

Physiological and autonomic observations, like respiratory rate and heart rate variability, we measured using the BIOPAC system [35]. These physiological data will be analyzed in a separate paper.

- **VR stimulation and procedure**

The study included four 360-degree videos, each lasting up to 5 minutes, delivered through VR support. The VR experience was implemented using the Oculus Quest 2, a standalone virtual reality

headset equipped with a high-resolution display (1832 x 1920 pixels per eye), a refresh rate of up to 120 Hz, and a wide field of view to enhance immersion. The device's lightweight design and built-in tracking system enabled participants to interact with the virtual environment comfortably, without requiring additional external sensors. The videos included two familiar scenarios and two non-familiar scenarios. The videos were selected by the team of authors to provide contrasting yet equally immersive and emotionally engaging experiences.

The familiar scenarios consisted of relaxing beach landscapes in Sardinia, created using footage from a YouTube video (https://www.youtube.com/watch?v=6yAHk_0sv0Q). These videos were looped to depict calm, uninterrupted seaside environments without external interferences or people, aiming to evoke memories of Southern Italian beaches.

The non-familiar scenarios included a serene park in Japan, sourced from a YouTube video (https://www.youtube.com/watch?v=uaJdWd_n1lg), and a mesmerizing aurora borealis display, sourced from another YouTube video (https://www.youtube.com/watch?v=cg_jfip4pSQ).

These videos were paired with corresponding music: traditional Italian folk or melodic pop songs for the familiar scenarios, and non-familiar folk songs for the non-familiar scenario (Figure 2).
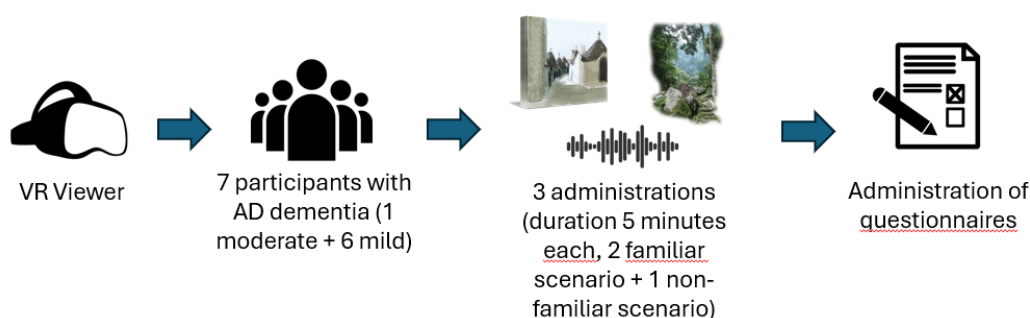

Figure 2. Schematic representation of the experimental paradigm. Participants (n = 7; 1 with moderate and 6 with mild Dementia due to AD) engaged in three virtual reality (VR) sessions using an Oculus Quest 2 VR viewer. Each session lasted 5 minutes and included exposure to two familiar scenarios (e.g., Italian beaches) and one non-familiar scenario (e.g., the aurora borealis or a Japanese park), accompanied by corresponding music. After each session, participants completed questionnaires to evaluate their experiences and emotional responses.

The selection of the songs was guided by an evaluation process conducted by a group of 4 musicians with expertise in musicology. The evaluation was based on a pool of 30 songs categorized into three groups: Italian lyric songs, Italian folk songs, and foreign compositions. The evaluation process considered several key dimensions for each song. Familiarity was assessed using a 5-point scale, where 1 indicated very low familiarity (the participant did not know the song at all) and 5 indicated very high familiarity (the participant knew the song well or found it reminiscent of similar genres or melodies). Arousal was also rated on a 5-point scale, with 1 representing very low arousal (the song elicited calmness and relaxation) and 5 representing very high arousal (the song evoked energy and excitement). Additionally, pleasantness was measured on a 5-point scale, where 1 indicated very low pleasantness (the song was not enjoyable) and 5 indicated very high pleasantness (the song was highly enjoyable and evoked positive feelings). The songs that were rated as the most relaxing and least activating were selected for the study to ensure they aligned with the calming and immersive goals of the VR intervention. The selected songs included "Non ho l'età" sang by G. Cinquetti, "Il cielo in una stanza" sang by G. Paoli, "Sogna fiore mio" performed by Lucilla Galeazzi, Marco Beasley, L'Arpeggiata,Christina Pluhar and composed by Ambrogio Sparagna, and "Vulesse addeventare nu Brigante" sang by Carlo D'Angiò and produced by Musicanova for the familiar scenarios, and "Finnish Chant" and "Japanese Sonata" for the non-familiar scenarios. A full list of the evaluated songs is provided in Supplementary Table 1.

Each participant was shown the two familiar scenarios and one of the two non-familiar scenarios paired with familiar or unfamiliar music (randomly assigned to the videos among the selected songs), with the order of presentation randomized as follows: one familiar scenario, followed by the other familiar scenario, and finally a non-familiar scenario.

3. Results

- **Behavioral data**

The following section provides a comprehensive overview of the results obtained from the SUS presence scale and the VAS.

All participants reported a high level of immersion in the virtual environment, with most perceiving the environment as realistic. According to the SUS and VAS questionnaire, half of the participants described the setting as resembling a documentary or an external space, while the other half felt as though they had personally visited the location. Notably, the participant with moderate cognitive decline perceived the environment as resembling a documentary and was aware of being in a virtual environment, contrasting with the responses of participants with mild cognitive decline, who were more likely to report a sense of personal immersion. Regarding mood changes, 3 out of 7 participants reported an improvement in mood following the experience, 3 maintained a positive mood throughout, and only 1 participant experienced a decline in mood, expressing feelings of sadness. This participant, who had moderate cognitive decline, attributed the sadness to the type of landscapes presented, describing them as isolated and reminiscent of once-lived spaces that now appeared abandoned. Tranquility was a prominent sensation, with 6 out of 7 participants reporting a sense of calmness, while one individual described feeling desolation.

In terms of side effects, 5 participants did not report any adverse effects. However, one participant experienced some anxiety related to aversive evoked memories associated with a scenario, as evaluated using the VAS. The VAS required participants to rate their mood on a scale from 0 (very happy) to 5 (extremely sad) before, during, and after the VR experience. The participant, the only one with moderate cognitive decline, exhibited a reduction in mood scores between the pre- and post-experience assessments. In the open-ended interview conducted afterward, this participant reported a state of anxiety triggered by certain scenarios. Another participant reported mental fatigue, attributed to the weight of the VR headset. These observations highlight potential limitations of an autobiographical approach, which should be considered in future studies and discussed further in the context of its applicability.

Concerning memory recall, 4 out of 7 participants experienced positive memories related to their childhood or adolescence, often tied to experiences with their parents or visits to places resembling those presented during the VR experience. The remaining 3 participants recalled recent positive experiences, also connected to similar environments depicted in the virtual scenarios. Notably, despite experiencing anxiety and sadness, the participant with moderate cognitive decline recalled a past episode during the viewing of the Tokyo-park scenario, where she and her mother used to play with her children.

In terms of feedback, 4 participants expressed a desire to explore more scenarios, 3 wished to move around or interact with the environment, and 3 (including the one with moderate cognitive decline) suggested improvements to make the VR headset lighter and more comfortable. One participant also expressed a preference for a greater variety of music.

4. Discussion

This study highlights the feasibility and potential benefits of employing Virtual Reality (VR) interventions for patients with mild to moderate cognitive decline compatible with MCI or dementia profile. The results demonstrate that immersive VR experiences, combined with emotionally evocative music, can elicit positive mood changes, evoke autobiographical memories, and provide a calming and engaging experience for most participants. Previous studies have highlighted the

potential of VR therapies in MCI and early AD for improving cognitive and physical functions [36]. Additionally, the integration of music therapy within virtual environments has shown promise in alleviating psychological and cognitive symptoms of AD [37,38].

Our findings expand on this by combining VR and music therapy, providing a multi-sensory therapeutic intervention. This unique approach demonstrates how multi-modal stimulation can enhance therapeutic outcomes, offering participants both cognitive and emotional benefits. Importantly, even a participant with a moderate cognitive decline, as evidenced by lower MoCA scores achieved meaningful results. For instance, despite experiencing some negative emotions such as anxiety and sadness, these individuals were able to recall significant autobiographical memories, highlighting the potential of VR to stimulate emotional and cognitive engagement even at more advanced stages of the disease [39]. Personalized and culturally relevant stimuli played a central role in eliciting these responses, emphasizing the importance of tailoring interventions to individual needs. Moreover, the aesthetically pleasing design of the VR scenarios contributed significantly to the intervention's overall appeal and effectiveness, enhancing user satisfaction and emotional resonance [40]. While minor side effects such as mental fatigue or discomfort were noted, they underscore the necessity of optimizing device design and content customization to improve usability and participant experience.

These observations underline the importance of further research to advance VR-based interventions. Future studies should investigate how integrating culturally sensitive and individually tailored content can amplify the therapeutic benefits of VR. Additionally, exploring long-term impacts, scalability, and the integration of VR with other therapeutic modalities could pave the way for more robust applications in diverse clinical contexts.

The current study has several limitations. Firstly, the small sample size limits the generalizability of the findings to the broader AD population. Secondly, the short-term nature of the intervention precludes conclusions about its long-term effects on mood, cognition, or quality of life. Additionally, participants were recruited via a service center rather than a neurology department, which limited access to formal dementia diagnoses. This recruitment method may have influenced the representativeness of the sample and the scope of clinical information available.

Moreover, the lack of a control group makes it difficult to determine whether the observed effects can be attributed solely to the VR intervention. The variability in participants' familiarity and comfort with technology may have also influenced the outcomes. Finally, the subjective nature of some measures, such as participant feedback, may introduce bias.

However, it is important to note that this is a feasibility study, and these limitations are more pertinent to intervention studies, which are beyond the scope of the current research. Instead, specific methodological limitations associated with feasibility studies should be considered. For example, this study lacks certain standardized measures, such as usability assessments like the SUS, which are often recommended in VR research to evaluate user experience and interface effectiveness [41]. Additionally, the absence of objective physiological metrics to assess engagement and stress levels during VR exposure is often considered a limitation. However, in this study, we collected physiological data, including respiratory frequency and heart rate variability, alongside subjective assessments to provide a comprehensive understanding of VR's therapeutic potential. While the collection of these data alongside the VR immersion preliminary demonstrates the feasibility of the approach, these physiological measures have not been analyzed yet in order to first focus here on the overall illustration of the protocol, but will be explored in detail in a future paper. Such analyses will enhance methodological rigor and contribute to a more robust evaluation of the intervention's applicability [42].

Another limitation concerns the practical aspects of the VR system itself. The weight of the Oculus Quest 2 device may have caused discomfort during prolonged sessions, particularly for older participants, potentially impacting their overall experience. Additionally, the relatively high cost of VR equipment may limit its accessibility and scalability in broader clinical applications.

5. Conclusions

The positive results of this feasibility study provide a solid foundation for the design and implementation of larger-scale randomized controlled trials (RCTs) to validate the preliminary findings. Future RCTs should aim to assess the efficacy of VR interventions in improving cognitive and emotional outcomes in AD populations, with a particular focus on long-term effects. Building on the promising outcomes observed, further research could also explore the integration of VR with other non-pharmacological approaches, such as cognitive training or physical exercise, to potentially enhance its therapeutic impact. These next steps will contribute to establishing VR as an accessible and effective tool for cognitive rehabilitation in neurodegenerative conditions.

An important issue related to VR immersions using the Oculus device is its high cost and relatively bulky design, which may reduce its accessibility for widespread use. This limitation could be addressed in future studies by adopting VR visors compatible with mobile phones. These devices are not only more affordable but also portable and easier to use, making them more accessible for patients and their caregivers. As current VR technology allows the translation of Oculus-programmed scenarios to smartphone-compatible formats, this approach could facilitate the testing of this paradigm and other similar interventions in diverse settings, including home environments, thereby increasing its feasibility and practicality.

Lastly, developing tailored VR content that considers cultural and individual differences could optimize the intervention's effectiveness and accessibility. For example, VR scenarios could be adapted to reflect familiar landscapes or cultural landmarks relevant to specific populations, such as local parks, iconic monuments, or traditional environments. Additionally, incorporating language customization and culturally specific auditory cues (e.g., traditional music or ambient sounds) could enhance the user experience. Personalizing content based on individual preferences, such as serene natural scenes for relaxation or interactive tasks for cognitive stimulation, might further improve engagement and therapeutic outcomes [43].

In summary, while this study underscores the promise of VR as a complementary therapeutic tool for improving emotional well-being in AD patients, it is noteworthy that even participants with lower MoCA scores, indicative of moderate AD, demonstrated positive outcomes. Despite challenges such as anxiety and sadness, these participants recalled meaningful autobiographical memories, suggesting the potential of VR to evoke emotional and cognitive engagement even in more advanced stages of the disease. Furthermore, the aesthetic quality of the VR experience, characterized by its immersive and visually engaging content, contributed to its overall effectiveness and user satisfaction. These findings highlight the need for further research to refine and expand the clinical applications of VR, particularly in designing interventions that leverage the therapeutic benefits of aesthetic and emotionally evocative environments.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board (or Ethics Committee) of University of Bari (ET-24-18-R1, 17-07-2024).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The original contributions presented in this study are included in the article/supplementary material. Further inquiries can be directed to the corresponding author(s).

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

AD	Alzheimer's Disease
MCI	Mild Cognitive Impairment
VR	Virtual Reality
MoCA	Montreal Cognitive Assessment
CRIq	Cognitive Reserve Index Questionnaire
VAS	Visual Analogue Scale
SUS	Slater-Usoh-Steed Presence Scale
BPSD	Behavioral and Psychological Symptoms of Dementia
QoL	Quality of Life
RCT	Randomized Controlled Trial
ARIA	Amyloid-Related Imaging Abnormalities

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