

# Assessment of Computer Assisted Rehabilitation Environment (CAREN) System Use and Mood in Patients With Multiple Sclerosis

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**Background:** Depression is a common comorbidity in patients with multiple sclerosis (MS) and is associated with decreased quality of life. Identifying treatments that aid psychological and physical rehabilitation in patients with MS provides valuable information for interdisciplinary teams.

**Methods:** Seventy-five adults with MS who completed the Patient Health Questionnaire-9 (PHQ-9) and Patient-Reported Outcomes Measurement Information System (PROMIS) Global Health scale during routine physical therapy appointments where the (CAREN) system was used were studied. Data were retrospective and collected via patient-reported outcomes. Group comparisons used 2-sample *t* tests or Mann-Whitney *U* tests for continuous variables and Fisher exact tests for categorical variables. To examine self-reported depression, mean  $\pm$  SD baseline scores were computed and stratified by number of CAREN sessions.

**Results:** Patients with 5 or more sessions seemed to have lower baseline PHQ-9 and PROMIS Mental Health scores; however, no significant differences were found at the univariate level. There were no statistically significant differences in follow-up scores for the outcome measures.

**Conclusions:** Current research evaluating the rehabilitation of patients with MS using the CAREN system is scarce. This pilot study is important to inform prospective studies exploring use of the CAREN system for psychological rehabilitation. Patients with 5 or more CAREN sessions had lower baseline PHQ-9 scores, which may suggest that mood plays a role in the selection of patients for CAREN system use. This study shows that mood is not affected by the CAREN system. More specific research needs to be completed with a more robust sample. *Int J MS Care. 2022;24(2):63-66. doi:10.7224/1537-2073.2020-131*

Mood disorders are common in patients with multiple sclerosis (MS). The prevalence of depression is approximately 50% depending on the method used and the study population.<sup>1,2</sup> The lifetime prevalence of depression in patients with MS is approximately 3 times higher than that in the general population and exceeds that in other chronic diseases, including other neurologic disorders.<sup>1,3-6</sup> Current research suggests that the development of depression in patients with MS involves at least 3 mechanisms: (1) psychological reaction to disease, (2) inadequate coping, and (3) lesion burden to the central nervous system and

functional changes due to inflammation.<sup>1</sup> In addition, there is an understanding that use of MS therapies, corticosteroids, and spasticity medications is associated with high depression.<sup>7,8</sup> Therefore, depression is often considered both a reaction to and a symptom of MS.

The impact of MS on quality of life (QOL) has been well documented in the literature.<sup>9,10</sup> Compared with other chronic illnesses, MS has a greater effect on QOL due to its chronic progressive course.<sup>11</sup> The presence of depressive symptoms is one of the most critical predictors of QOL, with depression explaining more variance in QOL than disability status.<sup>12</sup>

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In addition, patients often report gait abnormalities among the most distressing consequences of MS, with limited mobility subsequently affecting independence and QOL.<sup>13,14</sup> Research has provided evidence that physical therapy can improve QOL in patients with MS.<sup>15</sup> As such, limited mobility is often a contributory factor to mood symptoms, and specifically, depression. It has been suggested that virtual reality, and specifically the Computer Assisted Rehabilitation Environment (CAREN) system, can be an effective adjunct treatment to decrease depression and increase QOL in patients with MS.

The CAREN system is an immersive virtual environment that provides a motivational and effective alternative to traditional rehabilitation for patients with MS.<sup>16</sup> The CAREN system is a high-tech medical and research system that allows medical experts to view and analyze balance, locomotion, and coordination in an interactive, controlled environment. With CAREN, rehabilitation experts, orthopedists, occupational therapists, physiotherapists, neurologists, and pediatric, mental health, and research experts collaborate using a multidisciplinary tool. The CAREN system uniquely immerses participants in a multisensory virtual reality experience that allows the registration, evaluation, clinical analysis, and rehabilitation of human balance, including the visual, auditory, vestibular, tactile, and proprioceptive systems of the body. The physical setup of CAREN involves a “6-degrees-of-freedom” motion base topped with force plates or an instrumented treadmill and a real-time motion capture system integrating visual projection and surround sound. The CAREN platform fully immerses the individual into an environment where visuals, the floor (which moves up and down, left and right, and turns), and the sound system combine and react to behavior. The user can easily create a variety of customized virtual environments for research and rehabilitation purposes. The CAREN system is able to provide real-time feedback. In addition, many rehabilitation therapists use the ability of the CAREN system to complete dual tasks during the session, including cognitive dual-tasking or a physical task while also walking. The real-time feedback is a significant benefit that provides instantaneous results for both the therapist and the patient, contributing to the immersive environment of the CAREN system.

Owing to the small number of CAREN systems in use, there has been little scientific evidence of its effectiveness for mood and QOL.<sup>16</sup> Virtual reality has been shown to benefit balance impairments, physical activity, and level of functioning.<sup>17</sup> The CAREN system may be more motivational in nature compared with traditional physical therapy due to the repetitive nature of traditional rehabilitation.<sup>16</sup>

Virtual reality, and specifically the CAREN system, may provide psychological advantages to traditional rehabilitation services, such as providing clearer goals, greater task concentration, and clearer immediate feedback.<sup>16,18</sup> Therefore, the CAREN system may be associated with a positive effect on patients’ mood and subsequent QOL while also contributing to effective physical and cognitive rehabilitation.

Identifying treatments that aid in reducing mood symptoms while also increasing functionality in patients with MS could have an important effect on their care. More extensive studies evaluating the ability of systems, such as the CAREN, to treat symptoms associated with MS, including mood symptoms, are needed.<sup>17-19</sup> In addition, the need to examine treatments that positively associate with a reduction in psychiatric symptoms are needed in the MS population. The present study explored the potential psychological benefits of the CAREN system in a subset of the MS population. To our knowledge, this is the first study to examine depression in the context of treatment using the CAREN system in patients diagnosed with MS.

## Methods

### Participants and Design

Patients in this historical cohort were chosen for study by retrospective review of medical records. All the patients attended the Cleveland Clinic Mellen Center for Multiple Sclerosis for care between January 1, 2013, and December 31, 2018. Inclusion criteria included age 18 years or older and, due to the pilot nature of the study, at least 1 physical therapy session using the CAREN system. Patients were excluded if they did not complete the Patient Health Questionnaire-9 (PHQ-9)<sup>20</sup> and the Patient-Reported Outcomes Measurement Information System (PROMIS) Global Health scale before and after the physical therapy appointments using the CAREN system. Use of the PHQ-9 has been determined to be valid in the assessment of depression symptoms in the MS population.<sup>21</sup> Approval was obtained by the Cleveland Clinic internal institutional review board and ethics board. The need for informed consent was waived.

### Statistical Analysis

Descriptive statistics (eg, means, SDs, medians, interquartile ranges, frequencies, percentages) for demographic and clinical variables recorded at baseline were computed for the entire cohort and stratified by number of CAREN sessions (1-4 vs 5 or more). Group comparisons were performed using 2-sample *t* tests or Mann-Whitney *U* tests for continuous variables and Fisher exact tests for categorical variables.

To examine self-reported depression and QOL in patients with MS using the CAREN system, mean  $\pm$  SD baseline

scores were computed, again for the full cohort and stratified by number of CAREN sessions. Similar tests as mentioned previously herein were performed to determine whether baseline scores varied by group as defined by number of sessions. In addition, we created linear regression models in which the baseline score was the dependent variable. Categorized number of CAREN sessions was the independent variable, and variables found to be statistically significantly associated with group were included as covariates.

To compare pre-post psychological self-report scores after trial of the CAREN system, we created separate linear regression models (one for each score). The last score recorded during the course of treatment was the dependent variable, and the corresponding baseline score was included as a covariate. Again, variables found to be statistically significantly associated with group were included as covariates.

Because this study is exploratory in nature, correction for multiple testing was not performed, but interpretation of the results will be made in light of the number of tests being performed. All computations were performed using R version 3.5.0 (R Core Team),<sup>22</sup> and  $P < .05$  was considered statistically significant.

## Results

A total of 75 patients with MS used the CAREN system during the study period and were chosen for study. Patient characteristics for the entire cohort and stratified by number of CAREN sessions are presented in **Table S1**, which is published in the online version of this article at IJMSC.org. Mean  $\pm$  SD patient age was  $51.5 \pm 14.5$  years; 66.7% were women and 68.0% were of White race. Compared with patients with 1 to 4 CAREN sessions, patients who had 5 or more sessions were older ( $P = .029$ ), had MS for a longer period ( $P = .037$ ), and were more likely to be taking escitalopram oxalate ( $P = .038$ ). Although patients with 5 or more CAREN sessions seemed to have better baseline PHQ-9 and PROMIS Mental Health scores, no significant differences were found at the univariate level (**Table S1**).

Results of linear regression models for baseline scores are presented in **Table 1**. After adjusting for age, time since diagnosis, and use of escitalopram oxalate, there were no statistically significant differences in baseline scores for any of the outcomes (PHQ-9, PROMIS Physical, PROMIS Mental Health).

Results of linear regression models for follow-up (ie, posttreatment) scores are also presented in **Table 1**. After adjusting for age, time since diagnosis, use of escitalopram oxalate, and the corresponding baseline score, there were no statistically significant differences in follow-up scores for any of the outcomes (PHQ-9, PROMIS Physical, PROMIS Mental Health).

**Table 1. Baseline and Follow-up Scores Comparing Patients With 5 or More CAREN Sessions With Patients With 1 to 4 CAREN Sessions**

Score	Estimate (95% CI)	P value
Baseline		
PHQ-9 (n = 48)	-0.8 (-4.9 to 3.3)	.694
PROMIS Physical (n = 29)	1.6 (-5.7 to 9.0)	.650
PROMIS Mental Health (n = 29)	4.0 (-4.9 to 12.8)	.365
Follow-up		
PHQ-9 (n = 36)	1.3 (-1.1 to 3.6)	.282
PROMIS Physical (n = 15)	4.8 (-5.7 to 15.2)	.328
PROMIS Mental Health (n = 15)	4.5 (-4.8 to 13.8)	.298

CAREN, Computer Assisted Rehabilitation Environment; PHQ-9, Patient Health Questionnaire-9; PROMIS, Patient-Reported Outcomes Measurement Information System.

## Discussion

Current research evaluating the rehabilitation of patients with MS using the CAREN system is scarce. Although no statistically significant differences were found between or within groups, this pilot study is an important step to inform perspective studies exploring use of the CAREN system and other types of virtual reality for psychological rehabilitation. Previous research suggests that the CAREN system creates a more engaging environment for therapy.<sup>16-19</sup> Given the more engaging environment, it has been suggested that there is a decrease in depression. The current pilot study's results are unclear regarding this suggestion.

Patients with 5 or more CAREN sessions seem to have a lower baseline PHQ-9 score, which may suggest that mood plays a role in the selection or participation of patients using the CAREN system. More specifically, patients who have lower levels of depression may be selected more frequently to use the CAREN system. A possible explanation for this finding is that patients

## PRACTICE POINTS

- There is scarce research examining use of the Computer Assisted Rehabilitation Environment (CAREN) system for psychological and physical rehabilitation in patients with MS.
- There is opportunity to investigate the impact of the CAREN system on various facets of psychological functioning.
- Additional research is needed to clearly delineate the ways that virtual reality can be used as an adjunctive treatment for psychological functioning.

experiencing less depression may be more likely to volunteer to trial the CAREN system. Recent research has suggested that physical disability has been associated with higher depression in MS.<sup>13,14</sup> Therefore, patients with higher levels of depression may not be able to physically use the CAREN system for physical rehabilitation.

There were multiple limitations to the study given the retrospective methods and limited sample size. The limited sample size likely contributed to the lack of statistically significant associations between the number of CAREN sessions and scores. Given the results and limitations, future prospective studies are needed to evaluate what types of patients would benefit from CAREN-based therapies, including adjunctive treatment of mood symptoms prevalent in the MS population. In addition, a prospective study is warranted to address the previously noted limitations. Capturing mood-related data immediately after a CAREN session is likely a more effective method for assessing the impact of the CAREN system on psychological functioning. Future research should also specifically measure the impact of the CAREN system on reported QOL measurements. Furthermore, future considerations should also include individuals who have not taken an antidepressant in the past 3 months of the study.

Although the investigation of using the CAREN system as an adjunctive intervention for mood is in its infancy, this study provides some context to explore additional ways to provide treatment from an interdisciplinary perspective. The unpredictability of MS may result in significantly greater variability of depression scores from physical therapy session to physical therapy session. Therefore, perhaps the psychological advantages of using the CAREN system may be more related to engagement, joy, or flow as opposed to traditional depression symptoms. Additional investigation as to how the CAREN system can address both physical and psychological rehabilitation should not be deterred by the results of this pilot study. Given the anecdotal evidence of patient report after using the CAREN system, there is likely to be a psychological advantage. □

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