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## Single Case – General Neurology

# Virtual Reality Training Helpful in Motor and Cognition in Corticobasal Syndrome: A Case Report PET Study

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## Keywords

Corticobasal syndrome · Virtual reality · Atypical Parkinson syndrome · PET · Case report

## Abstract

Corticobasal syndrome (CBS) is a rare progressive neurodegenerative disease characterized by a combination of asymmetric motor symptoms and non-motor symptoms. CBS is poorly responsive to levodopa. Non-pharmacological strategies have been found to be useful as components of a multidisciplinary therapeutic approach for patients with CBS. The purpose of this study was to investigate the effects of virtual reality training in addressing symptoms of CBS. A 64-year-old man was clinically diagnosed as CBS one year after the onset of complaints. Positron emission tomography (PET) scan showed asymmetrical hypometabolism in the right thalamus and basal ganglia. The patient was evaluated for balance, gait, mobility, and cognition 1 week before, 1 week after, and 1 year after 6 weeks of training, 3 times weekly (18 sessions in total). All clinical outcomes and PET result had improved after the intervention; cognition and balance were maintained after 1 year. Additionally, the asymmetric hypometab-

olism, which had been detectable on the PET scan, became normal, and a relative improvement was noted in the visual evaluation of cortical involvement. Virtual reality may address different aspects of motor and cognition and possibly brain metabolic changes that can affect the course of the disease in patients with CBS.

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Published by S. Karger AG, Basel

## Introduction

Corticobasal syndrome (CBS) is a rare progressive neurodegenerative disease characterized by a combination of asymmetric motor symptoms (bradykinesia, akinesia, rigidity, postural instability, and falls) and non-motor symptoms (apraxia, agnosia, and cognitive impairment) that respond poorly to levodopa [1, 2]. CBS is considered as atypical Parkinsonism and due to common symptoms with Parkinson's disease (PD), differential diagnosis between CBS and PD is a difficult clinical decision. While there are many treatment methods available for PD, limited literature exists for CBS. Currently, there are no disease-modifying treatments and approved pharmacological or therapeutic approaches that are effective in controlling symptoms in CBS. In terms of motor symptoms, especially bradykinesia and rigidity, levodopa may provide some improvements, but evidence is contradictory, and the benefit is often negligible and short-term [3]. Similarly, acetylcholinesterase inhibitors and N-methyl-D-aspartate receptor antagonists have been used open label for impairment in cognitive function, but evidence of their effectiveness is limited, and the risk of side effects may overcome the benefits [3]. In addition, non-pharmacological strategies have been found to be useful as components of a multidisciplinary therapeutic approach for patients with CBS [4].

Virtual reality (VR)-based treatment methods and exergaming (EG) have been found to improve motor and cognitive symptoms in PD [5–7]. The better and superior effects of VR and EG compared to the conventional rehabilitation methods have been shown in PD [8–11], and VR technology may be beneficial in neurorehabilitation. The purpose of this case report is to show the effects of VR-based EG (VR-EG) in improving symptoms of CBS.

## Case Description

A 64-year-old, right-handed man reported to the outpatient neurology clinic at Istanbul Medipol University Hospital, one year after the onset of complaints including impaired balance, frequent falls during transitional movements, disturbances in the activities of daily living, and cognition. The patient reported difficulties in walking for long distances and problems in controlling balance accurately. He was walking without freezing of gait, but he was “stuck” on several occasions during walking and dragging his left foot. The motor subscale of the Movement Disorders Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) was used to rate the motor symptoms of the disease severity (MDS-UPDRS-III) and the score was noted as 19 at baseline. Positron emission tomography (PET) scan showed asymmetrical hypometabolism in the right thalamus and basal ganglia. The patient was clinically diagnosed as CBS according to the latest consensus diagnostic criteria. This study reports the required

information regarding CARE guidelines (online suppl. additional file 1; for all online suppl. material, see [www.karger.com/doi/10.1159/000508492](http://www.karger.com/doi/10.1159/000508492)).

### *Intervention*

An oral and written informed consent was obtained from the patient before inclusion in the study. The patient had no experience with VR training and EG. VR-EG was applied 3 times per week for 6 weeks (18 sessions in total) using a Nintendo Wii Fit Balance Device. Nintendo Wii Fit Plus games including gait, static, and dynamic balance were applied during every session lasting for 1 h. The main selection criteria for the games were applicability and safety of the games [12]. He was encouraged to progress into the advanced levels that would need more concentration and mental execution and consequently imply challenges with higher cognitive and motor demands.

The patient's medical treatment was under the supervision of a neurologist and not modified during the study. Prescribed medications regulated by the neurologist included 75 mg levodopa, 18.75 mg carbidopa, and 200 mg entacapone three times a day plus 800 mg piracetam three times a day. Additionally, the patient was advised to adopt a gluten-free diet in daily life as far as possible [13].

### *Outcome Measures*

All assessments took place 1 week (T0) before, 1 week (T1) after, and 1 year (T2) after the intervention. The intervention and related assessments were performed by an experienced physical therapist. Outcome measures were Montreal Cognitive Assessment (MoCA), Timed Up and Go test (TUG), 6-Minute Walk Test (6MWT), The Activities-specific Balance Confidence (ABC), Berg balance scale (BBS), and PET scan. The procedures of the PET scan are given in online supplementary additional file 2.

## **Results**

Motor and cognitive clinical outcomes had improved, and the patient reported to feel more confident in daily activities after the intervention and during the follow-up. Family education played an important role in the adherence of the patient to the treatment. However, the entertaining nature of the intervention was helpful in enhancing the adherence to the treatment sessions. No adverse effect or results were reported during the study. Performances in TUG and 6MWT improved immediately after the intervention, but declined during the follow-up session, although both follow-up values (T1 and T2) had improved compared to baseline (T0). The patient's balance had improved, and his confidence rate had increased. Both measures were maintained one year after the intervention. Finally, MoCA showed remarkable improvement in cognition after the intervention which was maintained during the follow-up evaluation (Table 1). Performances at the different time points are given in Figure 1.

PET scan analysis revealed a normalization of the asymmetrical hypometabolism in the right thalamus and basal ganglia. Additionally, a relative improvement was noted in the visual evaluation of cortical involvement (Fig. 2).

## Discussion

To the best of our knowledge, this is the first study on the beneficial effects of VR-EG on clinical and brain metabolic changes in a patient with CBS. VR-EG improved our patient's functions both in the motor and cognitive aspects after 6 weeks of rehabilitation; results that could be maintained for 1 year after the intervention. Additionally, improvement was observed in the brain metabolic activity after the intervention. VR-EG may have helped the patient to improve balance, cognition, and short-term gait and mobility, despite the degenerative nature of the disease.

While the patient continued on a stable dose of medication, and considering the progressive neurodegeneration, decline in gait and mobility assessment results after 1 year can be related to the deteriorating nature of the disease. Additionally, according to a remarkable balance performance during the follow-up session, it can be hypothesized that the patient may have adopted a decreased gait speed as a compensatory mechanism to improve balance. Interestingly, he reported his balance to be superb and satisfactory but complained about the tiredness after walking for two kilometers during the follow-up session.

Non-pharmacological treatments have been used in the treatment of CBS as part of a multidisciplinary approach, and patients may benefit from different forms of conventional and non-conventional approaches [4]. Research focusing on the benefits of rehabilitation is mostly limited to case reports, due to the rarity of CBS [14]. Previous case reports have demonstrated various forms of intervention in patients with CBS. Two recent case reports have reported on the effects of videogame-based mechanical training for the rehabilitation of the upper extremities and also on the effects of adapted tango on mobility and cognition in CBS [15, 16].

Nintendo Wii has been reported to improve motor and cognitive symptoms in PD [6, 17], and it can be used as a new technology in the rehabilitation of patients with CBS. VR-EG includes benefits from different principles of experience-dependent neuroplasticity such as high repetition rate, feedback, and motivation [18] and is found to be helpful in enhancing cognitive skills in older adults [19]. By implementing cognitive functions in motor skills, patients would need to focus and try to increase their attention to be successful in the games. Similarly, planning for the upcoming game tasks can induce their executive functioning. Meanwhile, because of the on-time visual feedback related to all movements and balance performance, probably better motor outcomes can be achieved. Finally, as dramatic improvements in PD symptoms have been reported following a gluten-free diet [20], changes in the dietary habits could play an important part of the multidisciplinary approach in addressing symptoms of CBS.

## Conclusion

VR-EG may address different aspects of motor, cognition, and possibly brain metabolic changes that may affect the course of the disease in patients with CBS. However, further randomized controlled studies with larger samples are needed to compare these effects with conventional forms of rehabilitation.

## Acknowledgement

We acknowledge Istanbul Medipol University Hospital, neurology outpatient clinic. Also, we thank our patient for giving us permission to report his clinical data.

## Statement of Ethics

This study was approved by the Non-invasive Clinical Research Ethical Committee of Istanbul Medipol University, and the study protocol has been approved by the Institutional Review Board. Written informed consent was obtained from the patient to publish his case, results, and images.

## Conflict of Interest Statement

No potential conflict of interest was reported by the authors.

## Funding Sources

The authors received no specific funding for this work.

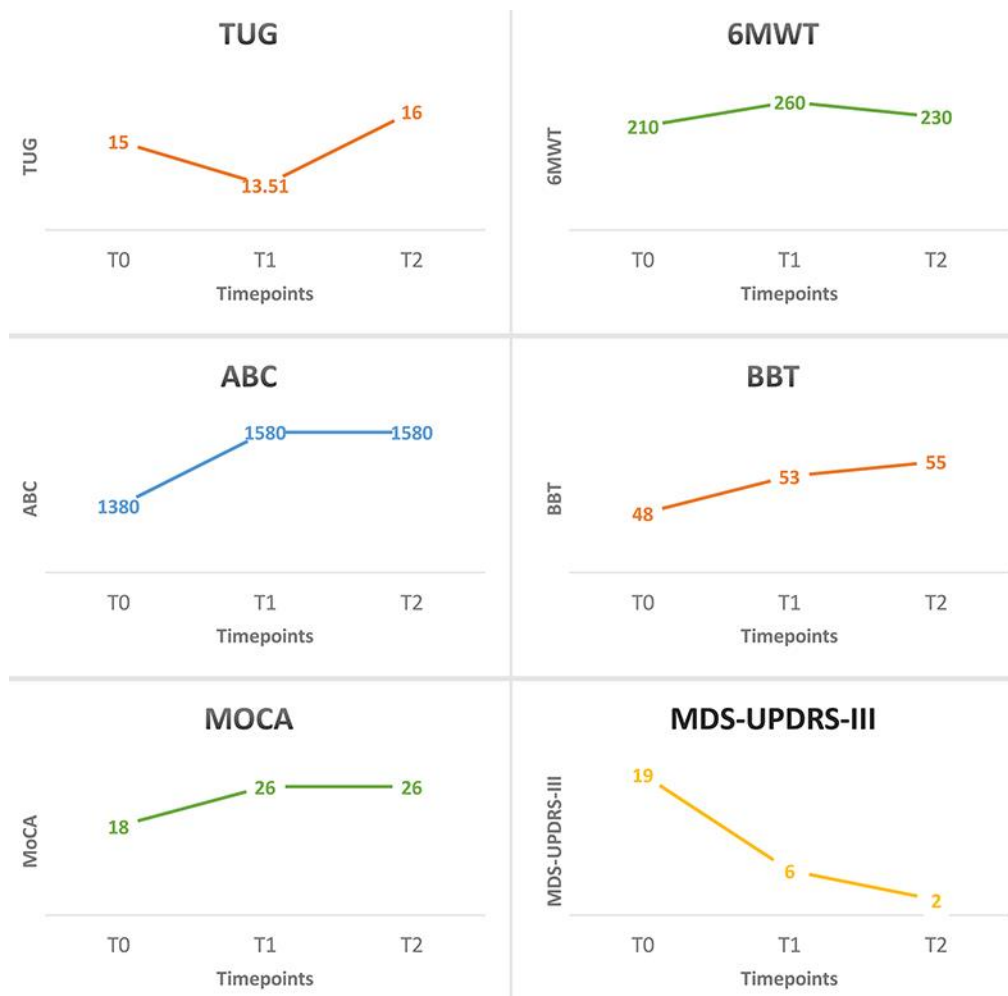
## Author Contributions

F.H. and L.H. developed the original concept of the case report, design, and methodology of the protocol. F.H. drafted the original manuscript. T.C. performed and interpreted the PET analysis and prepared PET results and figures. All authors reviewed and commented on drafts of the manuscript. All authors read and approved the final manuscript.

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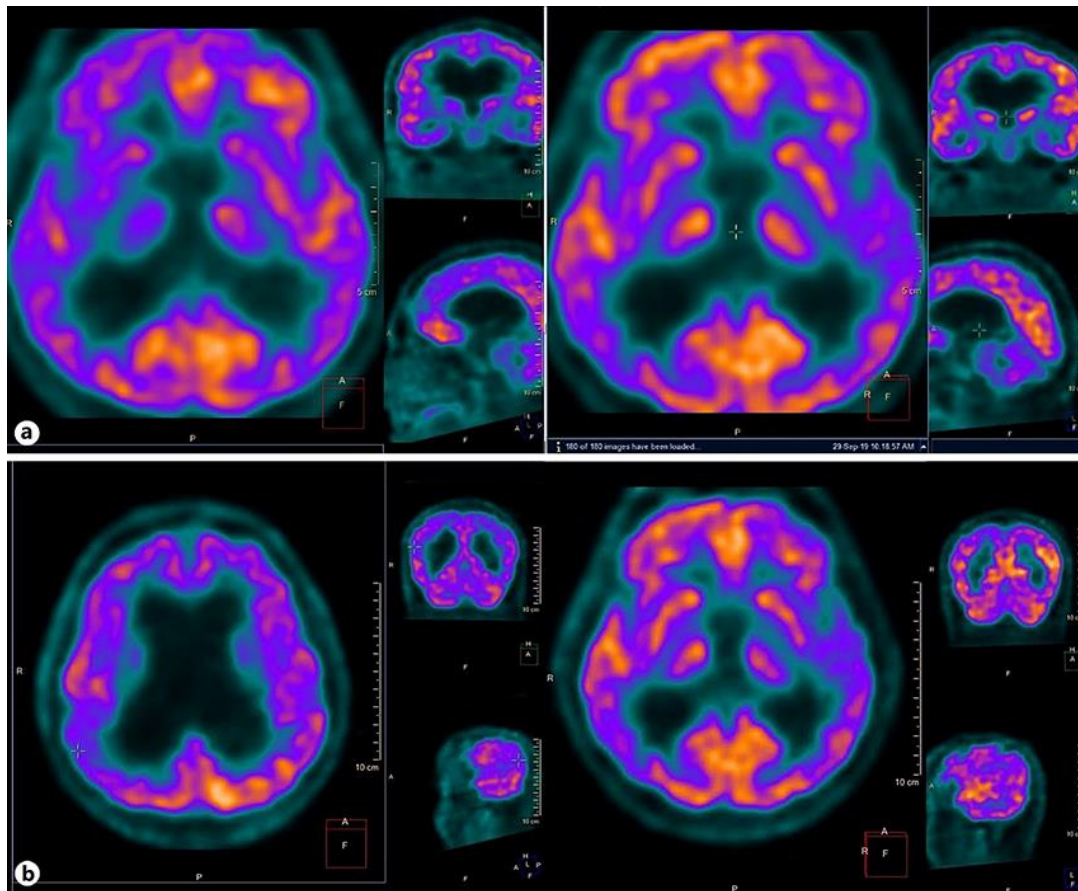
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**Fig. 1.** Test performances at the different time points: T0, 1 week before the intervention; T1, 1 week after the intervention; T2, 1 year after the intervention. Virtual reality-based exergaming may have helped the patient to improve balance, cognition, and short-term gait and mobility, despite the degenerative nature of the disease.





**Fig. 2.** Pre-intervention and postintervention results of PET scan: improvements were observed in the brain metabolic activity after virtual reality-based exergaming. PET scan analysis revealed a normalization of the asymmetrical hypometabolism in the right thalamus and basal ganglia. A relative improvement was noted in the visual evaluation of cortical involvement.



**Table 1.** Pretreatment (T0), posttreatment (T1), and follow-up (T2) results of clinical outcomes

Measurement	T0	T1	T2
TUG	15	13.51	16
6MWT	210	260	230
ABC	1,380	1,580	1,580
BBT	48	53	55
MoCA	18	26	26
MDS-UPDRS-III	19	6	2

All clinical measures had improved after the intervention (at T1 and T2). Follow-up assessments showed improvements in ABC, BBT, MoCA, and MDS-UPDRS-III. However, 6MWT had not improved after 1 year but maintained progressing compared to baseline. Improvement in TUG was not maintained until 1 year after the intervention. 6MWT, 6-Minute Walk Test; ABC, The Activities-specific Balance Confidence; BBT, Berg balance scale; MDS-UPDRS-III, Movement Disorders Society Unified Parkinson's Disease Rating Scale – motor subscale; MoCA, Montreal Cognitive Assessment; TUG, Timed Up and Go test.