

Research Report

A Virtual Reality-Based Screening Test for Cognitive Impairment in Small Vessel Disease

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Accepted 21 January 2021

Pre-press 9 February 2021

Abstract.

Background: There is a need for new practical tools to assess the cognitive impairment of small vessel disease (SVD) patients in the clinic.

Objective: This study aimed to examine cognitive functioning by administering the Virtual Supermarket (VST) in patients with SVD with cognitive impairment (SVD-CI, N = 32), cognitively normal SVD (SVD-CN, N = 37), and age- and education-matched healthy controls (HC, N = 30).

Methods: The tablet-based VST application and comprehensive traditional pencil-and-paper neuropsychological tests assessing memory, attention, executive function, visuospatial function, and language were administered to all participants.

Results: A moderate correlation was found between the “Duration” and “Correct Quantities” variables of VST and visuospatial function and general cognitive status composite Z scores across SVD-CI patients. “Duration” and “Correct Money” variables were moderately related to memory, executive functions, and visuospatial function composite Z scores across SVD-CN patients. A combination of all VST variables discriminated SVD-CI and HC with a correct classification rate of 81%, a sensitivity of 78%, and a specificity of 84%.

Conclusion: This study is the first to evaluate cognitive functions employing the VST in SVD with and without cognitive impairment. It provides encouraging preliminary findings of the utility of the VST as a screening tool in the assessment of cognitive impairment and the differentiation of SVD patients from HC. In the future, validation studies of the VST with larger samples are needed.

Keywords: Cognitive testing, small vessel disease, vascular cognitive impairment, virtual reality, virtual shopping task

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INTRODUCTION

The term cerebral small vessel diseases (SVD) refer to a group of pathological processes with various etiologies affecting cerebral small arteries, arterioles, veins, and capillaries resulting from the damage of deep gray and white matter [1]. According to conventional magnetic resonance imaging (MRI) findings, signs of SVD are small subcortical infarcts, white matter hyperintensities, lacunes, cerebral microbleeds, and brain atrophy [2, 3]. The presence of these signs has been reported to be a predisposing factor for the development of dementia and cognitive impairment [4, 5]. Many studies showed that SVD is characterized by impairments in executive functions, information processing speed, attention, working memory, visuospatial functions, language, and delayed memory [6, 7].

Cognitive impairment depends on the type, size, strategic location, and radiological evidence of the SVD [8]. Diffusion tensor imaging (DTI) studies have shown that extensive white matter structural damage, including lacunar infarcts, white matter hyperintensities, and brain atrophy, contribute to cognitive impairment [9]. It is emphasized that SVD pathologies disrupt cortical and subcortical networks that function in cooperation with each other, finally causing a disconnection syndrome [8]. These subcortical structures project and receive tracts from the prefrontal cortex [10]. The relationship between impaired prefrontal cortex connections and executive functions in SVD provides evidence showing the effect of disruption in networks on cognition [9].

In SVD, cognitive impairments are associated with deterioration in daily living activities. Furthermore, physical impairment, in addition to cognitive impairment in SVD, also greatly affects performance in both instrumental daily life activities such as shopping, working, and basic activities of daily life such as eating and dressing [11–13]. Cognitive impairment in SVD has a high incidence and burden for patients, their relatives, and health systems.

A detailed neuropsychological assessment is essential to detect cognitive impairment in SVD and can help the diagnosis of SVD. Even so, a brief cognitive test is needed as an alternative to an extensive assessment. Pencil-and-paper based screening scales such as the Mini-Mental State Examination (MMSE), the Montreal Cognitive Assessment (MoCA), and the Vascular Assessment Scale-Cognitive subscale are commonly used to evaluate cognitive impairment in SVD [14]. At that stage, there is a need for a practi-

cal tool for detecting executive dysfunction in SVD. The Virtual Supermarket Test (VST) was designed as a screening tool to detect mild cognitive impairment (MCI). VST is a tablet-based, easy-to-administer and quick virtual reality-based assessment tool, available in both self-administered and examiner-administered versions. The VST is associated with cognitive performance in visual and verbal memory, spatial navigation, attention, and executive function. In the Turkish and Greek sample, VST has been reported to have a correct classification rate of over 80% for MCI detection in older adults with and without subjective memory complaints [15–17].

To our knowledge, there is no study examining virtual reality-based or computerized cognitive assessment tools in SVD patients in previous literature. Therefore, the first aim of this study is to examine whether the VST can be used as a screening tool to detect cognitive impairment in SVD. The second aim is to investigate whether the VST correlates with traditional pencil-and-paper neuropsychological tests.

MATERIALS AND METHODS

Participants

Sixty-nine SVD patients and 30 healthy controls (HC) were recruited from the outpatient stroke clinic at Dokuz Eylul University Hospital, between the dates of January 1, 2016 and November 1, 2017. All participants underwent neurological examinations, an MRI scan of the brain, a neuropsychological test battery, and the VST. The Ethical Committee of the Dokuz Eylul University approved the study protocol. All participants were Turkish-speaking people and gave informed consent to the protocol.

The MRI (1.5 Tesla Philips Achieva scanner, Philips Medical Systems, Best, The Netherlands) of all participants was graded according to modified Fazekas Scale [18] by a neurologist. The periventricular hyperintensities was graded as; 0: no periventricular hyperintensities, 1: caps or pencil-thin lining in the frontal or occipital cap or lateral ventricular wall, 2: smooth halo surrounding lateral ventricles, and 3: irregular periventricular hyperintensities. Also, the deep white matter hyperintensities were scored as; 0: no deep white-matter hyperintensities, 1: focal or symmetrical point foci, 2: foci tend to converge, and 3: large conjoining foci.

The SVD patients were included in the study 3 months after stroke due to possible acute effects of stroke on cognitive performance. The inclusion cri-

teria for the enrollment of the SVD were as follows; Fazekas score ≥ 1 MRI; neurological diagnosis of SVD; MMSE score > 24 ; Geriatric Depression Scale score < 12 ; had no diagnosis of dementia according to dementia criteria in DSM-IV [19] and stroke associated with large vessel involvement or cardioemboli.

The SVD patients with cognitive impairment (SVD-CI) who scored lower by at least 1.5 standard deviations than age-and-education adjusted norms, in one or more cognitive domains and maintain their life activities independently were included in SVD-CI group [14]. The SVD patients with normal cognitive test scores according to age-and-education adjusted norms were included in the cognitively normal SVD patients (SVD-CN).

Exclusion criteria for SVD patients included psychiatric and neurological diseases other than SVD, and motor weakness that could prevent use of the VST.

The inclusion criteria for HC were having no large vessel disease or SVD as evidenced by MRI, and normal neuropsychological test performance, whilst the exclusion criteria were any history of psychiatric and neurological diseases.

Neuropsychological assessment

The neuropsychological test battery used consists of the Turkish version of revised MMSE [20, 21] for general cognitive status; Oktem Verbal Memory Processes Test [22] and Wechsler Memory Scale-Rev-

ised (WMS-R) Visual Reproduction Subtest [23] for visual and verbal memory; Stroop Test [24], Clock Drawing Test [25], phonemic fluency (F-A-S) [26, 27], Wechsler Adult Intelligence Scale-III (WAIS-III) Similarities Subtest [28], Luria Alternant Sequences Test [29] for executive function; Digit Span [23] for attention; figure copying test for visuospatial function; Boston Naming Test [30] and semantic fluency [26, 27] for language. Furthermore, the Beck Anxiety Inventory (BAI) for anxiety symptoms [31, 32], Geriatric Depression Scale (GDS) for depression symptoms [33, 34], and the Lawton Instrumental Activities of Daily Living (IADL) [35] were administered to all participants.

All raw scores of neuropsychological tests for all participants were converted to composite Z scores of neuropsychological domains including general cognitive status, memory, attention, executive function and visuospatial skills, and their means and standard deviations are presented in Table 1.

Administration of the VST

The VST has been described in detail previously [15, 16]. Briefly, the VST, developed by the Centre for Research & Technology Hellas/Information Technologies Institute (CERTH/ITI) in Association with the Greek Association of Alzheimer's Disease and Related Disorders (GAADR) as a screening MCI detection, is modeled on a daily shopping task. The VST is designed to be administered on a PC or an An-

Table 1
Clinical and demographical features of participants

	HC (N = 30)	SVD-CN (N = 37)	SVD-CI (N = 32)	<i>p</i>	SVD-CN versus HC	SVD-CI versus HC	SVD-CN versus SVD-CI
Age (y)	67.27 ± 7.79	62.73 ± 10.16	67.16 ± 9.35	0.071 ^a	NS	NS	NS
Education (y)	9.83 ± 3.73	9.30 ± 3.88	7.81 ± 3.58	0.066 ^a	NS	NS	NS
Gender (M/F)	11/19	25/12	10/22	0.014^b	<0.05	<0.05	NS
Fazekas (0/1/2-3)	30/-/-	0/35/2	0/19/13	<0.001^b	<0.05	<0.05	<0.05
MMSE	29.13 ± 1.07	29.08 ± 1.03	27.88 ± 1.43	<0.001^a	NS	<0.001	<0.001
IADL	17.0 ± 0.0	17.0 ± 0.0	16.61 ± 0.95	0.006^a	NS	0.020	0.012
GDS	6.74 ± 4.05	6.09 ± 5.48	5.67 ± 5.40	0.726 ^a	NS	NS	NS
Neuropsychological domains							
General Cognitive Status	0.32 ± 0.83	0.28 ± 0.80	-0.64 ± 1.10	<0.001^a	NS	<0.001	<0.001
Memory	0.78 ± 0.56	0.45 ± 0.55	-1.03 ± 0.66	<0.001^a	NS	<0.001	<0.001
Executive Function	-0.16 ± 0.58	-0.33 ± 0.61	0.40 ± 1.38	0.006^a	NS	NS	0.006
Attention	0.15 ± 0.82	0.009 ± 0.94	-0.16 ± 1.24	0.475 ^a	NS	NS	NS
Language	0.27 ± 1.17	0.35 ± 0.84	-0.59 ± 0.72	<0.001^a	NS	0.001	<0.001
Visuospatial	0.29 ± 0.31	0.24 ± 0.38	-0.46 ± 1.41	0.001^a	NS	0.002	0.003

SVD-CN, small vessel disease cognitively normal; SVD-CI, small vessel disease with cognitive impairment; HC, healthy control; SD, standard deviation; MMSE, Mini-Mental State Examination; IADL, Lawton-Brody Instrumental Activity of Daily Living Scale; GDS, Geriatric Depression Scale, ^aOne-Way ANOVA, ^bPearson Chi-Square. The mean and standard deviations of features and the *p*-values in pairwise comparisons with Bonferroni correction are presented.

droid® tablet. In this study, the VST was administered to all participants on a 10-inch Android® tablet. There are two versions of the VST: self-administered and examiner administered. In this study, the examiner-administered version was used [17].

The VST measures visual and verbal memory, attention, executive function, spatial navigation and has four difficulty levels (1–4), and the number and variety of items the user must locate and buy in the virtual environment differ at each difficulty level [15]. In the version used in this study, a different shopping list appears on the screen each trial to mitigate learning effects.

At the VST, the participant is given a shopping list and is expected to place the items on this list in the shopping cart quickly and accurately and complete the shopping. Then, the user is expected to pay the correct amount for these products at the cashier desk. VST measures five variables: “Correct Items”, “Correct Quantities”, “Bought Unlisted”, “Correct Money”, and “Duration”. The scores of these variables are calculated automatically.

The “Correct Items” variable is scored according to whether the participant correctly bought the item types requested in the shopping list. The “Correct Quantities” variable is calculated based on whether the participant buys the correct number of items in the shopping list. The “Bought Unlisted” variable is scored based on whether the participant bought different items than the requested items in the shopping list. The “Correct Money” variable is scored based on whether the participant has paid the correct amount for the items placed in the shopping cart. The “Duration” variable is measured by the time needed by the participant to complete the VST. While the “Duration” variable was recorded in the data set in seconds and minutes, other variables, except the “Duration”, were recorded as true or false, that is, as nominal variables.

The participants were first informed on how to use the VST and the use of the VST was demonstrated to them by a neuropsychologist. Then, the VST application was administered to all participants twice at difficulty level 1 with help by a neuropsychologist. Later, all participants completed the VST at difficulty level 2 with no help. The administration of the VST takes approximately 15–20 min.

Statistical analysis

IBM® SPSS 22.0 package was used for analysis. Clinical and demographic features, composite Z scores

of cognitive domains, and duration of the VST were compared with one-way ANOVA. Chi-Square test for nominal variables of the VST including “Correct Types”, “Correct Quantities”, “Bought Unlisted”, and “Correct Money” was used to examine the difference between SVD patients and HC. In pairwise comparisons, p -values were presented with Bonferroni correction. The relationship between categorical variables of the VST and neuropsychological domains was examined by Point-biserial correlation analysis, and the relationship between the continuous variable of the VST, “Duration” variable, and composite Z scores of neuropsychological domains was analyzed by Pearson correlation analysis in each group. Fisher’s Linear Discriminant Function analysis was used for levels of the correct classification rate, specificity and sensitivity of VST variables.

RESULTS

Clinical and demographical features in SVD patients and HC

The demographic and clinical features of groups are summarized in Table 1. Although there were no significant differences between SVD patients and HC in age ($F(2, 96) = 2.725, p = 0.071$) and education ($F(2, 96) = 2.791, p = 0.066$), GDS ($F(2, 96) = 0.321, p = 0.726$), there were significant differences in gender ($\chi^2 = 8.533, p = 0.014$), Fazekas ($\chi^2 = 116.950, p < 0.001$), MMSE ($F(2, 96) = 11.594, p < 0.001$), and IADL ($F(2, 96) = 5.430, p = 0.006$) scores. In addition, 53.5% of the participants had no experience of using technological devices such as tablet or smartphones.

SVD-CI patients displayed lower performance than HC in cognitive domains of general cognitive status ($p < 0.001$) and memory ($p < 0.001$), language ($p = 0.001$) and visuospatial functions ($p = 0.002$). The SVD-CI patients displayed poorer performance compared to SVD-CN in general cognitive status ($p < 0.001$), memory ($p < 0.001$), executive function ($p = 0.006$), language ($p < 0.001$), and visuospatial skills ($p = 0.003$). The SVD-CN patients and HC were similar in terms of neuropsychological test performance. Mean and standard deviations of composite Z scores of cognitive domains and p -value of pairwise comparisons with Bonferroni correction are presented in Table 1.

Table 2
VST variables among the SVD patients and HC

VST variables	HC	SVD-CN	SVD-CI	<i>p</i>	SVD-CN versus HC	SVD-CI versus HC	SVD-CN versus SVD-CI
Correct Types	100%	92%	78%	0.015^a	NS	<0.05	NS
Correct Quantities	90%	92%	75%	0.098 ^a	NS	NS	NS
Bought Unlisted	18%	18%	65%	0.007^a	NS	NS	<0.05
Correct Money	97%	92%	72%	0.008^a	NS	<0.05	NS
Duration (min)	5.96 ± 1.63	5.35 ± 3.05	9.63 ± 3.55	<0.001^b	NS	<0.001	<0.001

VST, Virtual Supermarket Test, ^aChi-Square, ^bOne-way ANOVA with Bonferroni correction. Correct response percentages of “Correct Types” “Correct Quantities” and “Correct Money” variables, incorrect responses percentages of “Bought Unlisted” variable and mean of “Duration” variables among groups are presented.

VST variables

There were significant differences between the three groups in terms of “Correct Types” ($\chi^2 = 8.418$, $p = 0.015$), “Bought Unlisted” ($\chi^2 = 9.880$, $p = 0.007$), “Correct Money” ($\chi^2 = 9.650$, $p = 0.008$), and “Duration” ($F(2, 96) = 20.061$, $p < 0.001$). However, there were no significant difference between groups in terms of “Correct Quantities” ($\chi^2 = 4.641$, $p = 0.098$).

Pairwise comparisons were made on all VST variables with adjusted *p*-values by Bonferroni correction. A significant difference was found between SVD-CI and HC in terms of “Correct Types” ($p < 0.05$), “Correct Money” ($p < 0.05$), and “Duration” ($p < 0.001$). In addition, there was a significant difference between SVD-CN and SVD-CI in terms of “Bought Unlisted” ($p < 0.05$) and “Duration” ($p < 0.001$). However, there was no significant difference between SVD-CN and HC in VST variables.

Percentages of correct responses in “Correct Types”, “Correct Quantities”, and “Correct Money” and incorrect responses in “Bought Unlisted” of VST variables and mean durations are presented in Table 2.

Discrimination analysis of VST variables and MMSE over groups

A combination of all VST variables displayed a CCR of 81% (78% sensitivity, 83% specificity) over SVD-CI and HC. Additionally, all VST variables distinguished between SVD-CI and SVD-CN with a CCR of 77% (83% sensitivity, 73% specificity). On differentiating between SVD-CN and HC, all VST variables had a CCR of 64% (65% sensitivity, 64% specificity). This data is presented in Table 3.

The MMSE displayed a CCR of 77% (74% sensitivity, 82% specificity) for discriminating between SVD-CI and HC. Discrimination results between

Table 3

Correct classification rate, sensitivity, and specificity of the VST variables and MMSE over groups

VST all variables	CCR %	Sensitivity %	Specificity %
SVD-CI versus HC	81	78	83
SVD-CI versus SVD-CN	77	83	73
SVD-CN versus HC	64	65	64
MMSE			
SVD-CI versus HC	77	74	82
SVD-CI versus SVD-CN	75	74	76
SVD-CN versus HC	52	56	46

CCR, correct classification rate.

SVD-CN and SVD-CI and SVD-CN and HC groups are presented in Table 3.

Correlations between VST variables and cognitive domains

Correlations between VST variables and composite Z scores of cognitive domains for SVD-CI and SVD-CN patients are displayed in Table 4. There were negative moderate and strong correlations between “Duration” variable and general cognitive status ($r = -0.374$, $p = 0.035$) and visuospatial functions ($r = -0.608$, $p < 0.001$) on SVD-CI patients. In addition, a positive moderate correlation was found between “Correct Quantities” and general cognitive status ($r_{pb} = -0.359$, $p = 0.044$) on SVD-CI patients. The “Duration” variable was positively correlated to memory ($r = -0.344$, $p = 0.037$), executive function ($r = -0.352$, $p = 0.047$), and visuospatial functions ($r = -0.534$, $p = 0.001$) on SVD-CN patients. The “Correct Money” variable was positively associated with executive function ($r_{pb} = -0.352$, $p = 0.035$) and negatively associated with visuospatial functions ($r_{pb} = -0.534$, $p = 0.001$) on SVD-CN patients. No significant correlation was found between VST variables and composite Z score of cognitive domains on HC.

Table 4
Correlations between composite Z scores of neuropsychological domains and VST variables on SVD-CI and SVD-CN patients

Cognitive domains	VST variables				
	Correct Types ^a	Correct Quantities ^a	Bought Unlisted ^a	Correct Money ^a	Duration ^b
SVD-CI					
General Cognitive Status		0.359*			-0.374*
Visuospatial					-0.608**
SVD-CN					
Memory					-0.344*
Executive Function				0.352	0.352*
Visuospatial				-0.534**	-0.534**

*Correlation is significant at the 0.05 level (2-tailed); **Correlation is significant at the 0.001 level (2-tailed);

^aPoint-biserial correlation; ^bPearson correlation.

DISCUSSION

This study tested the hypothesis that the VST can discriminate SVD-CI, from both SVD-CN patients and HC, and correlates with traditional neuropsychological tests. The VST accurately classified SVD-CI and HC with a CCR OF over 80%, and it was associated with general cognitive status, executive functions, memory, and visuospatial functions. The VST may be a screening test candidate for the detection of cognitive impairment in SVD.

Cognitive impairment in SVD is a commonly seen feature of the disease, and its detection can provide a great contribution to patient care, outcome prognosis, and management of pharmacological or non-pharmacological therapy such as referral to a cognitive exercise program. However, a detailed neuropsychological assessment takes a long time and requires a trained neuropsychologist [14]. New sensitive screening tests as an alternative to extensive neuropsychological assessments are needed to detect cognitive impairment in SVD. A few screening tests are widely used to evaluate cognitive impairment in SVD. The MMSE [20], one of the brief screening tests, evaluates the general cognitive state, but it is rather sensitive to Alzheimer's type of dementia. In addition, the MMSE has a weakness in assessing executive functions [36]. Two studies have shown that the MOCA is more sensitive than the MMSE in detecting cognitive impairment due to its additional evaluation of psychomotor speed and executive functions [37, 38]. One of these studies found that the sensitivity of the MOCA was 76.7% and specificity was 81.4% in differentiating vascular cognitive impairment patients from patients with the subcortical ischemic vascular disease without cognitive impairment [37]. In a study using The Brief Memory and Executive Test to detect

cognitive impairment in SVD, the rates of sensitivity and specificity of this pencil-and-paper cognitive screening test were 93% and 76%, respectively [39]. These tests as alternative screening tools for cognitive impairment in SVD can be administered in a short amount of time and allow healthcare professionals to use them with minimal training. To the best of our knowledge, the present study is the first in which a virtual reality tablet-based application, the VST is used to detect cognitive impairment in SVD. In the current study, we found that the tablet based VST distinguished SVD groups from HC with a better correct classification rate than the MMSE which is the most used cognitive screening test. Therefore, the VST can be a good alternative screening test for evaluation of cognitive impairment in SVD. On the other hand, it did not reach successful classification rates for the discrimination of SVD-CN and SVD-CI groups. Other advantages of the VST include: 1) its short duration of administration compared to traditional neuropsychological tests, 2) its ability to assess multiple cognitive domains such as executive functions, visuospatial functions, information processing speed, and memory, 3) the ease of administration and scoring on a tablet, and 4) familiarity and attractiveness of the shopping test mimicking daily life. However, it bears a disadvantage for individuals who are not familiar with new technologies such as tablets and smartphones. However, we observed high rates of successful test completion in our participants who did not have a prior experience with this technology.

The VST variables included "Correct Types" "Correct "Quantities" "Bought Unlisted" "Correct Money" and "Duration". SVD-CI patients had poorer performance than HC in "Correct Types" and "Correct Money" variables of the VST. Also, SVD-CI

patients showed lower performance in “Bought Unlisted” variable compared to SVD-CN. SVD-CN and HC were similar in performance on the VST (Table 2). The VST examines executive function, global cognitive functioning, spatial navigation, learning and memory [15–17]. Some studies have shown the existence of impairments of processing speed and executive function in SVD [11, 40, 41] and these impairments are related to the poor performance of instrumental activities of daily life such as a shopping activity [42]. In the current study, SVD-CI patients have completed the VST in longer duration than HC, and SVD-CN patients have finished the VST slower than HC. SVD-CN patients, the asymptomatic group of SVD, differed from HC only in terms of time needed to complete to the VST, while their neuropsychological test scores were within the normal range according to age and educational norms. As, the “Duration” variable measures executive function, navigation and global cognitive functioning [15], our findings indicate a decrease in information processing in SVD patients [43]. In the current study, VST was demonstrated to correlate with general cognitive status and visuospatial functions in patients with SVD-CI, and memory, executive functions, and visuospatial functions in SVD-CN patients. No relationship was found in the HC group (Table 4). These findings indicate that the relationship between VST variables and cognitive domains and correlation models in each group is different. The SVD-CI group performed poorly in general cognitive state, memory, language, and visuospatial functions compared to HC and SVD-CN and executive functions compared to SVD-CN alone. A significant increase in the “Duration” of the VST and a lower performance in the “Correct Money” variable was found in the SVD-CI group compared with HC and SVD-CN (Table 2). Since the VST “Duration” and “Correct Money” variables differ in the SVD-CI group, it is plausible that only these two variables are related to the general cognitive state and visuospatial domains. These variables of the VST evaluate functions such as general cognitive functioning, information processing speed, and spatial navigation. Similarly, the same variables of the VST in SVD-CN group were associated with memory, executive function, and visuospatial domains. Although not statistically significant, the relatively low performance in memory, visuospatial and executive functions in the SVD-CN group in comparison to HC, may be cause of association between the VST and cognitive domains of classical tests.

All VST variables can differentiate SVD-CI from HC with a correct classification rate of over 80%. The discrimination capacity of the VST to distinguish SVD-CI patients from SVD-CN patients is greater than the MMSE but weaker than formal extensive neuropsychological tests (Table 3). Previous studies of our group report better correct classification rates of the VST than the MMSE in discriminating amnesic MCI patients from HC [15, 16].

Two meta-analysis studies on cognitive status of SVD patients showed that executive functions, delayed memory, information processing speed, language, visuospatial functions, reasoning, and attention performance were lower in comparison to controls [6, 7]. In the present study, SVD-CI patients showed lower performance in general cognitive status, memory, language, executive functions, and visuospatial functions than SVD-CN and HC; while SVD-CN patients displayed impaired executive functions compared to HC (Table 1). Our findings of widely impaired cognitive domains in SVD are consistent with previous meta-analysis findings [6, 7]. It has been reported that cognitive impairment in white matter diseases such as multiple sclerosis, aging, and SVD may result from the white matter ultrastructural damage demonstrated by the DTI method [8, 44, 45]. In older adults and SVD, decreased fractional anisotropy and increased anterior diffusivity were found in the white matter tracts [8, 46]. To fulfil cognitive tasks, the effective functioning of common brain networks connected by white matter tracts is required. It has been reported that pathologies associated with SVD affect functioning and cognition by disrupting these connections, causing a so called “disconnection syndrome” [8]. When radiologically and clinically symptomatic SVD patients are compared with controls, impairment in both global integration and localized efficiency of brain networks has been reported. The presence of the disruption in the prefrontal cortex connections may indicate a possible mechanism that may explain the impairment in executive functions seen in SVD with cognitive impairment [9]. Studies using the DTI method point to dysfunction in white matter connectivity and emphasize the contribution of disintegrated white matter tracts to the explanation of clinical symptoms in SVD [9, 10]. Although all these findings help to understand the cognitive impairments in SVD-CI, there is a lack of literature-supported evidence to understand the relationship between cognitive function and VST in patients with no clinical symptoms, namely SVD-CN patients in our study.

Limitations of this study include the unfamiliarity of participants with technological devices such as tablets or computers. This may pose a problem in populations with various cultural and educational background differences; it may affect the generalizability of our results. Furthermore, the Euro currency, which is unfamiliar for our participants, was used to pay the items in the VST. This may have added more cognitive complexity in addition to the task challenge of the VST.

CONCLUSION

This is a pioneer study to evaluate cognitive functions on SVD patients by using the VST as a virtual reality-based screening tool. We have shown that the VST can distinguish the SVD group with cognitive impairment from the HC. The VST correlates well with measures of neuropsychological domains. In future studies, the validity and reliability of the VST should be examined with larger samples of SVD patients.

ACKNOWLEDGMENTS

This work was supported by the Scientific and Technological Research Council of Turkey [grant numbers 216S242].

CONFLICT OF INTEREST

The authors have no conflict of interest to report.

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