

# Cognitive Functions of Patients with Post Stroke Depression: Comparative Study on Executive Functions, Processing Speed, and Episodic Memory

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## Abstract

**Background:** Post-stroke cognitive impairment (PCI) and depression (PSD) are among the most common sequelae of cerebrovascular accidents (CVA). The current study aimed to investigate the cognitive impairment of CVA and PSD patients in comparison with healthy controls (HC).

**Methods:** A total of 60 volunteers (mean age, 62.98 [SD=3.98], 48.3% male) were recruited, with 20 participants in each group. Participants completed several standardized assessments, including the Hamilton Depression Rating Scale, Mini-Mental State Examination, Abbreviated Mental Test, Patient Health Questionnaire-9, and Depression in old Age Scale. The neuropsychological part of the evaluation was designed to investigate executive functions, processing speed, and episodic memory.

**Results:** Analysis of variance revealed that the performance of all three study groups did not differ in easy tasks of spatial planning, working memory, and episodic memory. However, the PSD group performed medium difficulty tasks worse than the CVA patients and HC group. The HC group, on the other hand, exhibited better performance on complex tasks of these cognitive domains compared to other groups. Moreover, the complex tasks of spatial planning and medium difficulty tasks of working and episodic memory were able to distinguish between CVA and PSD groups. Additionally, the processing speed was found to be superior in HC group than both CVA and PSD groups ( $p < 0.05$ ).

**Conclusions:** The findings emphasize the importance of early identification and cognitive enhancement of CVA and PSD survivors. Innovative cognitive rehabilitation and psychological interventions targeting these populations are essential to advance long-term patient-centered outcomes in the management of CVA services.

**Keywords:** Cognitive Functions, Episodic Memory, Executive Functions, Post Stroke Depression, Processing Speed, Working Memory

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## Introduction

Cerebrovascular accident (CVA) is a significant medical condition characterized by a disruption of blood flow to the brain, resulting in permanent tissue damage caused by hemorrhagic, thrombotic, or embolic events. CVA is recognized as the third leading cause of mortality and morbidity worldwide (1, 2). Among all CVA cases, ischemic

strokes account for approximately 85%, while hemorrhagic strokes constitute 12% of cases (1).

The debilitating consequences of CVA, dementia, and depression are associated with a high burden of incapacity, which is far greater than that of cancer and cardiovascular disease (3, 4). Therefore, understanding the underlying mechanisms of CVA and its associated comorbidities is critical for developing effective prevention and treatment strategies.

Post-stroke depression (PSD) is a mood disorder that is commonly observed in patients after experiencing a CVA or stroke (5). The underlying causes of PSD are multifactorial and include factors such as the location of the CVA and disturbances in the neurotransmitter pathways (6). The impact of PSD can be significant, as it is associated with an increased risk of developing post-cognitive impairment (PCI) and can interfere with the rehabilitation of CVA patients in both the short and long term (7-9).

PSD is categorized into two major types: Major Depression and Minor Depression. The prevalence of major depressive disorder within three months after CVA ranges from 22% to 31% (approximately one-third of survivors) (8, 10-13), while this range is up to 47% in Iran (14). However, the reported rates of PSD vary widely depending on the population of the study, the number of depressive symptoms included in the studies, the evaluation tool applied, and the time since CVA (1, 7, 15, 16).

The consequences of PSD are significant, and include functional disability, longer hospital stay (17), low quality of life, poor physical and cognitive recovery, and increased mortality rates (18, 19). Moreover, PCI is a common sequela that occurs following CVA in approximately 50% of CVA survivors (20-22), even over the long-term (chronic phase) (22-27). In fact, PCI is more common in PSD patients at 12 months, with memory, attention, nonverbal problem-solving, and psychomotor speed being the most affected (7). The latent nature of this condition, combined with the current lack of quick cognitive screens that can be implemented in high-volume urgent CVA clinics, may lead to low detection and treatment (28), subsequently resulting in poor long-term functioning or progression to severe CVA.

Neurological and neuropsychological conditions have a significant impact on patients' lives, and their economic, social, and psychosocial outcomes cannot be overlooked (29). Among these conditions, CVA and PSD are prevalent and widely researched. Despite this, there is a lack of knowledge about the cognitive impairments of CVA survivors compared to PSD patients.

Previous studies have shown that CVA patients experience executive deficiencies and depression, which are often coexistent and associated with a worse prognosis (30). In contrast, PSD is characterized by memory dysfunctions, executive dysfunctions, poor processing speed of information, attention deficit, and visuoconstructional/visuoperceptual malfunctions (31-35). Executive dysfunction is a common and chronic cognitive impairment in the CVA population and may exacerbate other cognitive abilities, such as learning and memory (33-36). Furthermore, cognitive dysfunctions in PSD patients tend to worsen over time, whereas they typically stabilize or progress in most CVA patients (31).

The Cambridge Neuropsychological Test Automated Battery (CANTAB) is a computerized battery that has been shown to have equivalence reproducibility with traditional methods for detecting cognitive deficits in patients who have experienced a CVA (37). CANTAB has been validated as a reliable neuropsychological battery (38), comprising computer-based tasks that can be administered through a touchscreen platform

to assess various cognitive functions (39). The precision and sensitivity of CANTAB in detecting impairments of cognitive functions across the spectrum of condition types and severities have been well established (37, 40). Furthermore, CANTAB can detect even subtle cognitive deficits in sub-acute CVA, when traditional measures may not be appropriate (37).

The high prevalence, mortality rate, and negative repercussions of CVA and PSD underscore the importance of characterizing distinct neuropsychological profiles that can elucidate various cognitive dysfunctions associated with these conditions. Early recognition and rehabilitation of CVA, particularly in the chronic phase, and PSD are essential for guiding the selection of cognitive rehabilitation and psychological interventions. Moreover, such characterization can enhance the precision of medicine and treatment strategies, which may, in turn, improve long-term patient-centered outcomes and optimize the organization of CVA services.

The purpose of this study was to identify and compare the various cognitive functions (specifically executive functions, processing speed, and episodic memory) of patients with CVA and PSD. Based on the limited literature available on the assessment of cognitive impairments in CVA and PSD using the CANTAB, we hypothesized that 1) the executive functions (spatial planning and working memory) of PSD patients would differ from those of CVA survivors and healthy controls; 2) the processing speed of PSD patients would differ from that of CVA survivors and healthy controls, and; 3) the episodic memory of PSD patients would differ from that of CVA survivors and healthy controls.

## Methods

### Participants

In the present study, a total of sixty subjects were recruited from the Rofeideh Rehabilitation Hospital in Tehran, Iran, between January 2020 and February 2022. The study included 20 patients with CVA, 20 patients with PSD, and 20 healthy controls (HC) who were matched according to age, gender, education, handedness, CVA type, and time since CVA.

The inclusion criteria for both CVA and PSD groups were first-ever CVA (ischemic or hemorrhagic) diagnosed by a neurologist, aged 50-75 years old, in the chronic phase (more than three months after the onset of CVA), with MMSE score 18 or greater, AMT score eight or greater, Treatment as Usual (TAU), and able to provide written informed consent. PSD diagnosis was confirmed by a psychiatrist and a psychologist using SCID-5 and having HDRS scores higher than 17 at baseline, cross-validated by DIA-S score four or greater and PHQ-9 score ten or greater. Exclusion criteria for all groups included a history of Intellectual disability, Substance Use Disorder (SUD), cognitive disorders prior to CVA, post-stroke seizures, acute diseases, severe brain trauma, depression and other known psychiatric disorders prior to CVA, severe aphasia, and suicidal thoughts or intentions. The study

**Table 1.** Demographic and characteristics in PSD, CVA, and HC.

	PSD	CVA	HC	Test
Number of Subjects, N	20	20	20	-
Age (years)	63.00±3.71	63.60 ± 3.40	62.45 ± 3.44	ANOVA
Mean ± SD				F = 0.53; $\rho$ = 0.59
Gender	12-Aug	9-Nov	10-Oct	$\chi^2$ = 0.93; $\rho$ = 0.62
Men/Women, N				
Handedness	19/1	18/2	16/4	$\chi^2$ = 2.26; $\rho$ = 0.32
Right/Left				
CVA Type	8-Dec	16/4	-	FE
Ischemic/Hemorrhagic				$\chi^2$ = 1.90; $\rho$ = 0.30
Time since CVA (months)*	6.70 ± 1.45	6.10 ± 1.11	-	IT
				T = -1.46; $\rho$ = 0.15
Education (years)	6/05 ± 2.06	7.25 ± 3.17	7.85 ± 2.92	ANOVA
Mean ± SD				F = 2.21; $\rho$ = 0.11
HDRS	51.20 ± 10.11	10.65 ± 3.99	8.15 ± 3.13	ANOVA
				F = 273.48, $\rho$ < 0.01
MMSE	22.35 ± 2.56	22.9 ± 2.65	27.75 ± 1.20	ANOVA
				F = 35.18, $\rho$ < 0.01
AMT	9.35 ± 0.48	9.20 ± 0.41	9.50 ± 0.55	KW
				KW = 5.22, $\rho$ < 0.73
PHQ-9	20.75 ± 3.30	5.05 ± 1.95	4.50 ± 1.84	ANOVA
				F = 280.77, $\rho$ < 0.01
				KW
DIA-S	7.5 ± 1.05	2.90 ± 0.30	1.80 ± 0.41	KW= 53.47, $\rho$ < 0.01

PSD, post-stroke depression group; CVA, cerebrovascular accident group; HC, control group; FE, fisher's exact; IT, independent t-test; KW, Kruskal-Wallis one-way analysis of variance; HDRS, Hamilton Depression Rating Scale; MMSE, Mini-Mental State Examination; AMT, Abbreviated Mental Test; PHQ-9, Patient Health Questionnaire-9; DIA-S, Depression in old Age Scale.

\* months passed after CVA

protocol was approved by the ethics committee, and after obtaining written informed consent, demographic data were collected, and cognitive domains were measured using various assessment instruments, including CANTAB, applied in random order by a blinded psychologist. All participants were evaluated in the same quiet room, between 9:00 to 12:00 AM, using CANTABeclipse™ on a touch screen laptop with a press pad.

### Measures

The present study employed the Structured Clinical Interview for DSM-5 (SCID-5) (41) to evaluate patients' clinical presentations. Following the SCID-5 assessment, the initial diagnosis of major depressive disorder was established as PSD. In addition, the severity of depressive symptoms was evaluated using the Hamilton Depression Rating Scale (HDRS) (42) during the personal interview. This approach enabled a comprehensive evaluation of patients' depressive symptoms and informed the treatment plan accordingly.

Furthermore, we utilized the Patient Health Questionnaire-9 (PHQ-9) (43) to assess depression in a face-to-face interview. A PHQ-9 score of  $\geq 10$  indicates a diagnosis of major depressive disorder in the past two weeks, with scores ranging from 0 to 27. To optimize the cross-validity of PHQ-9, we administered the Depression Inventory for Screening (DIA-S) (44), which is designed as a screening tool for use in clinical settings, in accordance with the diagnostic criteria for depressive disorders outlined in the International

Classification of Diseases-10 (ICD-10) (45). This approach facilitated a comprehensive and reliable assessment of patients' depressive symptoms, which was crucial for designing and implementing effective treatment strategies.

In this study, we evaluated cognitive domains concurrently using the Mini-Mental State Examination (MMSE) and the Abbreviated Mental Test (AMT) as screening instruments for abnormal cognitive functions in the geriatric population of Tehran, Iran. The MMSE is a valid and reliable test for assessing cognitive impairment in older adults (46), while the AMT is a useful screening tool that has been shown to have high specificity and sensitivity (81.50% and 92.15%, respectively) at a cut-point of AMT<8 in Iranian elderly populations (47).

In addition to the MMSE and AMT, we also used four subtests from the CANTAB that are commonly affected in cerebrovascular accidents (38): One Touch Stocking of Cambridge (OTS), Spatial Working Memory (SWM), Reaction Time Index (RTI), and Paired Associates Learning (PAL).

OTS tests assess the function of the frontal cortex and executive impairment, while SWM evaluates the subject's capacity to retain spatial data and manipulate remembered factors in working memory, which is processed mainly within the dorsolateral prefrontal cortex (dlPFC) (48). PAL measures visual memory and new learning and is mainly sensitive to significant changes in medial temporal lobe functioning (38). The subject's speed of response to visual stimuli is assessed

**Table 2.** OTS test scores in PSD, CVA, and HC.

Test	PSD (n=20)	CVA (n=20)	HC (n=20)	ANOVA	Post hoc
OTS-MCC1	1.09 ± 0.16	1.03 ± 0.09	1.03 ± 0.08	F = 3.68; $\rho$ = 0.028	HC < PSD <sup>2,3</sup> PSD = CVA HC = PSD = CVA <sup>1</sup>
OTS-MCC2	1.12 ± 0.16	1.11 ± 0.17	1.04 ± 0.09	F = 3.00; $\rho$ = 0.054	HC = PSD = CVA <sup>1</sup>
OTS-MCC3	1.14 ± 0.21	1.11 ± 0.14	1.06 ± 0.11	F = 2.27; $\rho$ = 0.11	HC = PSD = CVA <sup>1</sup>
OTS-MCC4	1.39 ± 0.43	1.33 ± 0.35	1.22 ± 0.32	F = 2.06; $\rho$ = 0.13	HC < PSD <sup>1</sup>
OTS-MCC5	1.55 ± 0.41	1.48 ± 0.42	1.33 ± 0.27	F = 3.37; $\rho$ = 0.038	HC = CVA PSD = CVA HC, CVA < PSD
OTS-MCC6	2.09 ± 0.78	1.73 ± 0.50	1.45 ± 0.36	F = 10.67; $\rho$ < 0.001	HC = CVA <sup>2</sup>

PSD, post-stroke depression group; CVA, cerebrovascular accident group; HC, healthy control; OTS, One Touch Stocking of Cambridge; OTS-MCC1/2/3/4/5/6, mean choice to correct of 1/2/3/4/5/6 moves of OTS.

Low score denotes better cognition.

1 Bonferroni test was used for post hoc analysis.

2 Tamhane test was used for post hoc analysis.

3 HC<PSD indicates that the mean of groups HC and PSD significantly differ.

4 HC= CVA indicates that the means of groups HC and CVA do not differ significantly.

through RTI. It is important to note that the CANTAB-Eclipse has previously been shown to be sensitive to diagnosing mild cognitive impairments (MCI) (49). This instrument is highly standardized, reliable, user-friendly, and produces instant scoring (38).

Overall, the combination of these screening instruments allows for a comprehensive evaluation of multiple cognitive domains, providing a more nuanced understanding of cognitive impairment in the geriatric population of Tehran, Iran.

### Statistical Analysis

The data in this study were analyzed using the SPSS statistical platform (version 26.0 for Windows) by a biostatistician who was blinded to the study. Descriptive statistics were presented as the mean (M) and standard deviation ( $\pm$ SD). Categorical variables were analyzed using chi-square and Fisher's exact tests. The Student's independent t-test was applied to compare the means of the same variables in two groups when their distribution was normal. The normality of the distribution of continuous variables was evaluated using the Shapiro-Wilk test.

To compare the means of the PSD, CVA, and HC groups, one-way analysis of variance (ANOVA) was used for parametric data, while Kruskal-Wallis one-way analysis of variance (KW) was used for non-parametric data. For equal variances, Bonferroni's post hoc test was applied (Levene's test  $\rho$  > 0.05), while Tamhane's test was used for unequal group variances (Levene's test  $\rho$  < 0.05) to determine the significance of pairwise comparisons in one-way ANOVA. The significance level was set at  $\rho$  values < 0.05.

### Results

The present study aimed to compare cognitive performance among patients with PSD survivors of CVA, and HC using the CANTAB. The assessment of cognitive performance using CANTAB subtests lasted for a mean duration of  $45.25 \pm 14.20$  minutes (ranging from 21.76 to 101.62 minutes) across all participants. Notably, the evaluation took significantly longer in PSD and CVA patients compared to HC ( $52.03 \pm 13.24$ ,  $46.09 \pm 12.21$ , and  $38.80 \pm 7.46$  minutes, respectively); however, there were no significant differences in the testing time between PSD and CVA patients (ANOVA F = 11.88,  $\rho$  < 0.001).

Table 1 displays the demographic and clinical characteristics of the study participants. There were no significant differences between the groups with respect to age, gender, handedness, CVA type, time since CVA, education, and AMT scores ( $\rho$  > 0.05). As expected, significant differences were observed between the groups in terms of HDRS, MMSE, PHQ-9, and DIAS-S scores ( $\rho$  > 0.05).

Table 2 presents the results of the analysis of the mean choice to correct for different numbers of moves in the OTS subtest. The results indicate that the mean choice to correct for one, five, and six moves (OTS-MCC 1, 5, 6) were significantly higher in PSD patients compared to HC ( $\rho$  < 0.05). However, there were no significant differences in the mean choice to correct for two, three, and four moves (OTS-MCC 2, 3, 4) among the three groups ( $\rho$  > 0.05).

The results of the study demonstrated that the total errors of the SWM subtest, specifically SWM-TEs, were significantly higher in both patients with CVA and PSD when compared to HC ( $\rho$  < 0.001). However, there was no significant difference in the outputs of SWM-TEs between CVA and PSD survivors ( $\rho$  > 0.05). Moreover, the total errors of SWM-TEs 4 did not

**Table 3.** SWM test scores in PSD, CVA, and HC.

Test	PSD (n=20)	CVA (n=20)	HC (n=20)	ANOVA	Post hoc
SWM-TEs	33.03 ± 19.94	23.40 ± 19.02	11.37 ± 11.08	F = 14.85; $\rho < 0.001$	HC < CVA, PSD <sup>3</sup> PSD = CVA <sup>2,4</sup>
SWM-TEs 4	1.12 ± 1.94	0.90 ± 1.17	0.23 ± 0.57	F = 2.86; $\rho = 0.061$	HC = PSD = CVA <sup>1</sup>
SWM-TEs 6	8.58 ± 8.60	4.90 ± 6.31	1.93 ± 2.66	F = 9.53; $\rho < 0.001$	HC < PSD <sup>2</sup> HC = CVA PSD = CVA
SWM-TEs 8	23.18 ± 12.53	17.40 ± 12.35	9.13 ± 9.70	F = 14.17; $\rho < 0.001$	HC < CVA, PSD PSD = CVA <sup>1</sup>

PSD, post-stroke depression group; CVA, cerebrovascular accident group; HC, healthy control; SWM, Spatial Working Memory; SWM-TEs, total errors of SWM; SWM-TEs 4/6/8, total errors for 4,6 or 8 boxes of SWM.

Low score denotes better cognition.

1 Bonferroni test was used for post hoc analysis.

2 Tamhane test was used for post hoc analysis.

3 HC<PSD indicates that the mean of groups HC and PSD significantly differ.

4 PSD=CVA indicates that the means of groups PSD and CVA do not differ significantly.

show any remarkable difference among all three groups ( $\rho > 0.05$ ).

Similar to the aforementioned subtests, differences in SWM-TEs were more apparent with increasing complexity of the task in all groups. Notably, the output of SWM-TEs 4 did not indicate any noticeable difference among groups ( $\rho > 0.05$ ). When analyzing SWM-TEs 6, it was found that this factor was significantly higher in PSD survivors when compared to HC ( $\rho < 0.001$ ), whereas the output of CVA survivors was similar to HC and PSD patients ( $\rho > 0.05$ ). Finally, SWM-TEs 8 were significantly higher in both CVA and PSD survivors when compared to HC ( $\rho < 0.001$ ), while the results were not significantly different between CVA and PSD patients ( $\rho > 0.05$ ) (Table 3).

These findings suggest that both CVA and PSD patients exhibit impaired spatial working memory, with greater impairment observed in tasks with greater complexity. Moreover, the differences in SWM-TEs between CVA and PSD survivors were not significant, which implies that these groups may share similar cognitive deficits

The mean scores of simple reaction time (RTI-SRT), 5-choice movement time (RTI-FCMT), and 5-choice reaction time (RTI-FCRT) were significantly lower in HC when compared to both patients with CVA and PSD survivors ( $p < 0.05$ ). However, there were no significant differences in the mean scores of these factors between CVA and PSD survivors ( $p > 0.05$ ) (Table 4).

These findings suggest that both CVA and PSD survivors exhibit impaired reaction times when compared to healthy controls. However, there were no significant differences in reaction times between CVA and PSD survivors, which implies that these groups may share similar deficits in this regard. These results may have implications for the development of cognitive rehabilitation programs for CVA and PSD survivors.

The results of the study indicated that the total errors of the PAL subtest, specifically PAL-TEs, were significantly higher in both patients with CVA and PSD survivors when compared to HC ( $\rho < 0.001$ ). Notably, the data regarding the PAL-TEs at

levels with low numbers (PAL-TEs 1,2,3) were significantly better, and as the task complexity increased, there were no noticeable differences among the groups ( $\rho > 0.05$ ).

When analyzing PAL-TEs at the 6-figure level, it was found that HC and CVA survivors had significantly fewer errors when compared to PSD patients ( $p < 0.05$ ). Furthermore, at the 8-figure level, HC made significantly fewer errors than both CVA and PSD survivors ( $\rho < 0.05$ ), while the outputs in CVA and PSD patients did not show any significant difference (Table 5).

These findings suggest that both CVA and PSD patients exhibit impaired paired associates learning, with greater impairment observed in tasks with greater complexity. Additionally, the significant differences in PAL-TEs between HC and both CVA and PSD survivors imply that these groups have deficits in associative learning when compared to healthy controls. These results may inform future interventions for improving cognitive function in CVA and PSD survivors.

## Discussion

The present study aimed to investigate the cognitive functions of patients with CVA and PSD in comparison to HC, specifically in terms of executive functions (i.e., planning and working memory), processing speed, and episodic memory.

The OTS subtest is a measure of executive function, specifically spatial planning, as established in the Cognition (2006) study. Our study found that both CVA patients and HC performed the medium complexity tasks of the OTS subtest better than the easy tasks, with no significant difference between groups. However, CVA and PSD patients performed worse on the complex tasks compared to healthy controls. These results are consistent with prior research (34, 35, 50) and suggest that executive dysfunction and slowed processing speed are common in CVA and PSD patients.

Executive impairment, which is mainly processed in the prefrontal cortex (PFC), is a significant risk factor for the quality of life of individuals with CVA. Approximately 75% of CVA patients experience executive impairments (32, 51, 52). Additionally, attention and executive function are both

**Table 4.** RTI test scores in PSD, CVA, HC.

Test	PSD (n=20)	CVA (n=20)	HC (n=20)	ANOVA	Post hoc
RTI-FCMT	569.30 ± 182.95	563.00 ± 316.74	359.75 ± 76.25	F = 11.22; $p < 0.001$	HC < CVA, PSD <sup>2</sup> CVA = PSD <sup>1,3</sup>
	416.73 ± 99.74	377.73 ± 68.67	322.10 ± 47.85	F = 10.80; $p < 0.001$	HC < CVA, PSD CVA = PSD <sup>1</sup>
RTI-SRT	392.95 ± 95.46	368.29 ± 88.72	305.98 ± 43.06	F = 10.82; $p < 0.001$	HC < CVA, PSD CVA = PSD <sup>1</sup>

PSD, post-stroke depression group; CVA, cerebrovascular accident group; HC, healthy control; RTI, Reaction Time Index; RTI-FCMT, five-choice movement time of RTI; RTI-FCRT, five-choice reaction of RTI; RTI-SRT, simple reaction time of RTI.

Low score denotes better cognition.

1 Tamhane test was used for post hoc analysis.

2 HC<PSD indicates that the mean of groups HC and PSD significantly differ.

3 CVA=PSD indicates that the means of groups CVA and PSD do not differ significantly.

impaired in CVA patients (53, 54), and these cognitive functions are significantly impaired in CVA patients (55).

It is common for one or more neurotransmitter systems to be altered as a significant sequela of hemorrhagic or ischemic damage to the brain (56-58), which may lead to long-term cognitive deficits that make it difficult for patients to engage in higher intellectual functioning and may have additional behavioral consequences, such as drug abuse or drug-seeking behavior, as well as PSD (59).

The SWM subtest is a widely used tool for assessing working memory (38), which primarily relies on the dorsolateral prefrontal cortex (dlPFC) (48). In this study, we found that the easy tasks of SWM were not sensitive enough to distinguish the differences among all groups, as they were too simple. The complex tasks were challenging for both CVA and PSD survivors, and the spatial planning assessment tasks were not appropriate for evaluating changes between CVA and PSD patients. However, the medium complexity tasks were able to differentiate working memory deficiencies between CVA and PSD survivors.

Our findings are consistent with previous research by van Geldorp et al. (2013), who demonstrated that CVA patients exhibited working memory difficulties on both object-related and spatial subtests of the SWM task compared to healthy controls. In addition, Roussel et al. (2012) found mild working memory deficits in CVA survivors with frontal cortex damage. Their study emphasized the rehearsal process aspect of the phonological loop component of the verbal assessment, and less noticeable impairments in the spatial element of the working memory-focused tasks.

These results suggest that various anatomical regions are involved in the sub-dimensions of working memory. Moreover, functional magnetic resonance imaging (fMRI) studies have indicated the cerebellum's importance, particularly the corticocerebellar circuitry, for intact working memory (60). Overall, our findings support the notion that medium complexity SWM tasks are the most appropriate for evaluating working memory in CVA and PSD survivors, and future studies should consider including fMRI to investigate the neural correlates of working memory in these populations.

The present study aimed to assess the processing speed in HC, stroke survivors (CVA), and patients with CVA using the RTI subtest. Consistent with earlier (29, 61, 62), the results revealed that the processing speed was significantly better in HC than in CVA and PSD patients. These findings are in line with previous studies reporting processing speed and cognitive flexibility deficits in CVA patients (52).

Processing speed impairment is known to be a major consequence of CVA (36, 63-66). Moreover, cognitive impairments, particularly non-verbal problem-solving, attention, memory, and psychomotor speed, are more frequent in PSD patients at 12 months (7). Laakso et al. (2019) reported that CVA patients performed poorly compared to HC in various executive functions, including response inhibition, initiation, set-shifting, strategy formation, and processing speed. In contrast, there is a lack of studies investigating differences in processing speed between CVA and PSD survivors.

Several studies have examined the effect of hemisphere lateralization on processing speed following CVA. For example, Gerristen et al. (2003) found that CVA patients with left-hemisphere lesions performed better than those with right-hemisphere lesions in visuomotor decision times that required high demands on spatial attentional capacity. However, left-hemisphere-lesion patients were notably slower than HC only in the most complex tasks.

Another possible underlying neural mechanism for processing speed alterations following CVA may be the dysfunction of various neurotransmitter systems. Previous research has suggested that neurotransmitters such as glutamate, dopamine, and gamma-aminobutyric acid modulate processing speed in neuropsychiatric and normal states (67). However, there is limited research investigating the role of neurotransmitter dysfunction in processing speed impairments following CVA and further investigation is needed.

The PAL subtest is widely used to assess episodic recall memory and new learning abilities, which are primarily governed by the medial temporal cortex (38). In this study, we evaluated the performance of individuals with CVA, PSD, and HC on PAL tasks of varying complexity.

**Table 5.** PAL test scores in PSD, CVA, and healthy controls.

Test	PSD (n=20)	CVA (n=20)	HC (n=20)	ANOVA	Post hoc
PAL-TEs	17.63 ± 13.08	12.70 ± 9.60	6.77 ± 6.06	F = 10.15; $\rho < 0.001$	HC < CVA, PSD <sup>3</sup> CVA = PSD <sup>2,4</sup>
PAL-TEs 1	0	0	0	-	HC = CVA = PSD <sup>1</sup>
PAL-TEs 2	0.18 ± 0.62	0.23 ± 0.57	0.13 ± 0.51	F = 0.22; $\rho = 0.80$	HC = CVA = PSD <sup>1</sup>
PAL-TEs 3	1.17 ± 1.91	0.90 ± 1.40	0.63 ± 1.35	F = 1.06; $\rho = 0.35$	HC = CVA = PSD <sup>1</sup>
PAL-TEs 6	5.52 ± 5.04	3.27 ± 4.51	1.77 ± 1.98	F = 8.08; $\rho = 0.001$	HC < PSD <sup>2</sup> HC = CVA CVA = PSD
PAL-TEs 8	10.82 ± 8.99	8.47 ± 6.86	4.23 ± 3.64	F = 7.79; $\rho = 0.001$	HC < CVA, PSD CVA = PSD <sup>2</sup>

PSD, post-stroke depression group; CVA, cerebrovascular accident group; HC, healthy control; PAL, Paired Associates Learning; PAL-TEs, total error of PAL; PAL-TEs 1/2/3/6/8, total errors at the 1-,2-,3-,6-, and 8-figure stages of PAL.

Low score denotes better cognition.

1 Bonferroni test was used for post hoc analysis.

2 Tamhane test was used for post hoc analysis.

3 HC < PSD indicates that the mean of groups HC and PSD significantly differ.

4 CVA = PSD indicates that the means of groups CVA and PSD do not differ significantly.

Our results suggest that medium complexity tasks of PAL were better performed by both CVA and HC groups, but not by the PSD patients. However, the complex tasks were found to be too difficult to detect significant differences in episodic memory between the CVA and PSD groups, and may only be useful for evaluating differences between CVA and PSD survivors compared to HC. On the other hand, the easy tasks of PAL did not prove to be beneficial for distinguishing differences among all groups.

These findings are consistent with previous research indicating that episodic memory is impaired in a substantial percentage of CVA patients (68-70), which can contribute to functional disability (71). Memory difficulties in CVA survivors are a consequence of vascular damage to memory circuits and, in some cases, associated Alzheimer's disease (72).

These findings suggest that PAL tasks, particularly medium complexity ones, may be a useful tool for evaluating episodic memory in CVA survivors and HC. However, due to the lack of sensitivity of complex tasks for detecting differences between groups, the use of easy PAL tasks may not be recommended for distinguishing differences among all groups. Future studies could explore the use of other cognitive tests to assess memory function in CVA and PSD patients.

The impact of cortical and subcortical damage levels on memory function in patients with brain lesions, such as CVA survivors, has been the subject of investigation. Although a number of studies have explored the relative effects of cortical versus subcortical damage on memory functioning, few have directly compared them. Studies have shown that CVA patients with cortical damage tend to experience more severe memory impairments compared to those with subcortical damage (73, 74). This finding is not unexpected, given the critical role played by numerous cortical regions in episodic memory function.

The posterior cortical area of the medial temporal lobe is widely believed to mediate the contextual, associative, and

recollective aspects of episodic encoding and retrieval, while the hippocampus is central to encoding ongoing information, and the multimodal related regions of the posterior cortex are typically thought to be the site for long-term storage of episodic memories (75-77). However, imaging studies have revealed that prefrontal lobe regions also contribute to the network involved in episodic memory processing (78, 79). It is suggested that prefrontal regions may facilitate the (re)constructive and searching processes of encoding and retrieval through their inherent executive functions (80, 81).

The findings of the present study are consistent with previous research indicating that individuals who have experienced CVA or PSD exhibit deficits in multiple cognitive domains when compared to HC. While there is a paucity of research directly comparing the unique cognitive profiles of CVA and PSD patients, it is well-documented that executive functioning, attention, visuospatial ability, language, verbal fluency, and orientation are among the domains commonly impacted by cognitive impairment in (1).

One of the main limitations of the present study is the lack of control over the specific type of CVA and the location of the brain lesion, which needs to be addressed in future studies. Two studies have demonstrated an association between posterior cortical atrophy (PCA) and left-sided CVA (82, 83). However, there is evidence to suggest that other cognitive domains, such as attention, may also be affected in both CVA and PSD patient (84). Further investigation into the potential impairment of other cognitive functions in these conditions would be beneficial.

In summary, the findings of this study indicate that individuals with CVA and PSD exhibit significant cognitive impairment compared to HC. These results underscore the importance of early detection and cognitive enhancement for individuals with PSD, particularly in the chronic phase. It is crucial to develop novel cognitive rehabilitation and psychological interventions that specifically target populations with these

conditions to improve long-term patient-centered outcomes and enhance the organization of CVA services.

## Declarations

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This study did not receive any explicit financial support from governmental institutions or public funding sources.

### Conflict of interest

The authors hereby declare that the current investigation was conducted in the absence of any perceived or actual financial or commercial relationships that may be deemed as potential conflicts of interest.

### Author Contributions

The authors' contributions to this study were as follows: BGD contributed to the acquisition, analysis, and interpretation of the data, as well as the drafting of the manuscript. SS, MS, and RH were involved in the study's conceptualization and design, as well as the re-interpretation of the data, and the drafting of the manuscript. All authors provided critical feedback on the manuscript and approved the final version for publication.

### Authors' contributions

FN and MP came up with the idea for the paper, FN, SK, and AR drafted it, and FN, MP, FR, and ND helped to write it. All of the authors reviewed the article.

### Ethical approval

The study protocol adhered to the highest ethical standards and was approved by the Ethics Committee of the University of Social Welfare and Rehabilitation Sciences, Tehran, Iran (Approval No. IR.USWR.REC.1398.203). All the procedures, including subject recruitment, data collection, and analysis, were carried out in strict accordance with the relevant regulations and guidelines, such as the Declaration of Helsinki and the International Conference on Harmonization Guidelines for Good Clinical Practice. Prior to their inclusion in the study, all participants provided their informed consent, which was obtained in writing, and the study procedures were initiated only after the written informed consent was signed. The voluntary participation of the subjects is greatly appreciated and has been crucial in the successful execution of this research.

### Consent for publication

This manuscript has been approved for publication by all authors.

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