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Research Article

Premorbid Employment and Education as Predictors of Recovery in General Cognition ten Years After Stroke Onset - A Longitudinal Cohort Study

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Abstract

Background: We have recently demonstrated significant general cognitive recovery with delayed improvement of working memory 10 years after stroke in a unique longitudinal cohort.

Aim: This study investigated demographic and clinical characteristics relevant to improved cognitive functions 10-year after a first-ever stroke.

Materials and Methods: A prospective longitudinal cohort study was carried out in 38 middle-aged (mean age =54 at stroke onset) stroke survivors. Cognition was assessed thrice at one week, seven months, and ten years after the stroke. Working memory and visuospatial function were assessed with the Digit Span and Block Design subtests, respectively. General cognition was evaluated with the Mini-Mental State Examination at the two later time points. Multivariate linear regression was used to identify the variables that may significantly predict improved cognitive functions at 10-year follow-up.

Results: We found that having a full-time job prior to the stroke, suffering an ischemic (as opposed to a hemorrhagic) stroke, and having a university education predicted significantly superior general cognitive function 10 years after stroke (R^2 of 0.77, $p < 0.001$), while working memory and visuospatial function at 1 week after stroke significantly predicted their respective functions at 10-year follow-up (R^2 of 0.41, $p = 0.003$).

Conclusions: Our results indicate that premorbid employment status and higher education as well as having suffered from an ischemic rather than a hemorrhagic stroke might predict superior cognitive recovery among middle-aged individuals 10 years after stroke.

Key words: cognitive improvement; cognitive reserve; education; employment; longitudinal study; stroke

Introduction

Cognitive impairment is frequent among stroke survivors and contributes significantly to their disabilities [1, 2]. Various cognitive impairments – including in orientation, memory, abstract reasoning, visuospatial ability, verbal fluency, attention, processing speed, and language [3-5] – have been reported in both the acute [4] and chronic phase [2] after stroke. Stroke is also associated with the development of dementia [6]. A recent systematic review and meta-analysis demonstrated that greater cognitive impairment among individuals after stroke onset results in more severe limitations in their ability to complete both basic and complex activities of daily living and participate in work, social, and leisure activities [7]. These associations have been observed not only for general cognitive impairment, but also for various cognitive domains [7].

The severity of cognitive impairment and extent of recovery after stroke depend on each patient's premorbid capacity, as well as on the characteristics of the stroke. In addition to common vascular risk factors [8, 9], a recent study has demonstrated that having obtained higher education and having an occupation are associated with less cognitive impairment and a more rapid recovery of cognitive function after stroke [10]. This is consistent with a meta-analysis that found that having fewer years of formal education was positively associated with post-stroke cognitive decline [11]. The effects of education and occupation on post-stroke cognitive improvements might be explained by the notion of cognitive reserve [12], the brain's capacity to minimize the clinical manifestations of brain pathology [13, 14].

The results of studies on the effect of stroke subtype on post-stroke cognitive impairment have been inconsistent [15, 16]. A study that included 2847 patients showed that cognitive impairments are more common after lacunar infarct [17] and that a similar proportion of patients with lacunar and non-lacunar stroke have mild cognitive impairment or dementia up to four years after stroke [18]. Further, a recent Nor-COAST study demonstrated that cognitive impairments are common in all stroke subtypes, with impairment of attention being dominant among the subgroup of individuals with large artery disease and cardioembolic stroke [15]. Hemorrhagic strokes are less common than ischemic strokes and are associated with high mortality [19], which may explain the scarcity of cognitive data from hemorrhagic stroke patients.

We have recently demonstrated significant general cognitive recovery with delayed improvement of working memory 10 years after stroke in a unique longitudinal cohort comprising 38 middle-aged individuals (aged 18–65 at stroke onset) [20, 21]. Visuospatial function recovered earlier than working memory, with evidence of recovery already observed at 7 months, and remained stable at 10-year follow-up. Language disorder, as assessed with D-KEFS-FAS, showed no significant alteration over the 10-year follow-up [20]. However, such very long-term follow-up studies are rare, and alterations in cognitive impairment after stroke remain overlooked [2]. Our data on improvement in working memory among persons with stroke is consistent with the recent Nor-COAST study [15], which demonstrated improvements in working memory among both middle-aged and elderly stroke patients despite the fact that age-related decline in working memory has been well demonstrated [22]. Interestingly, a higher level of education and having an occupation were associated with more cognitive recovery after stroke in a KOSCO study [10]. Together with other studies, the results of our previous study [20, 21] suggested that full long-term cognitive recovery is possible in individuals after stroke. To our knowledge, no organized cognitive rehabilitation was provided after the initial hospitalization in the current cohort; thus, participants' struggle to be active and/or live independently in their daily lives may be a crucial element in their cognitive improvements. This is reason why we hypothesize various demographic and clinical characteristics in this unique cohort may play some roles in the cognitive improvements.

The current study aimed to investigate which demographic and clinical characteristics are important for cognitive recoveries in middle-aged first-ever stroke survivors. Based on the results of previous studies, the null hypotheses were that length of education, employment status before and after stroke, stroke subtype, and demographic data would have no predictive value on cognitive improvements at 10-year follow-up in this cohort.

Materials and Methods

Study design

This single-center study was a prospective, longitudinal cohort study of stroke survivors with three consecutive follow-ups over a 10-year period after a first-ever stroke. The cognitive functions of stroke survivors were assessed prospectively at 10-year follow-up, then compared retrospectively with data collected one week and seven months after the time of stroke.
Ethical approval was obtained from the regional Ethical Review Board in Umeå, Sweden, D-nr 2015/144-31.

Recruitment and participants

The study was conducted at the Department of Neuro-Rehabilitation, University Hospital of Umeå. All middle-aged patients (18 to 65 years of age at the time of stroke) who had suffered a first-ever stroke between January 2004 and December 2007 and undergone neuropsychological assessments (NPA) at one- and 7-month after stroke. These data were collected from the medical journal. Only 10-year assessments were carried out prospectively. The participants were informed about the study and provided with written consent forms via letter, and research staff made contact with all eligible patients via telephone to improve the recruitment rate. Patients with severe dementia, severe aphasia, severe comorbidity, recurrence of stroke or transient ischemic attack, or other physical or psychiatric disease after first-ever stroke, along with those who were not community dwelling adults, were excluded [20]. After a thorough recruitment process taking place from 2015 to 2016, 49 of the total 102 middle-aged first-ever stroke patients with acute NPAs declined to participate and 15 others were excluded for a variety of reasons (Figure 1). Thus, our study included 38 stroke survivors with previous NPAs, all of whom provided their written, informed consent to participate in the 10-year follow-up. All were native Swedish citizens.

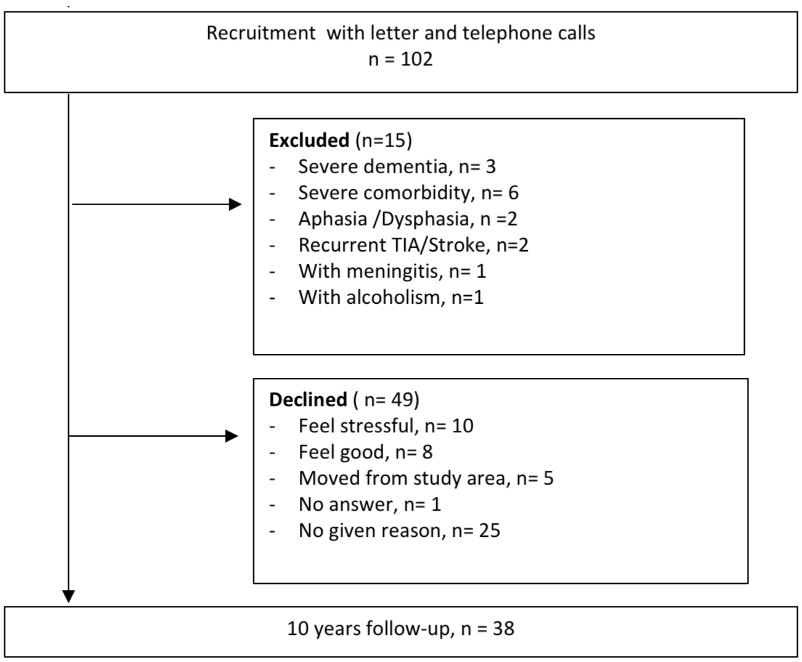

Figure 1: *Flowchart showing inclusion process*

Basic demographic and clinical characteristics

Baseline data were collected from the Riksstroke registry and patients' medical records. The clinical data, premorbid education level, and employment, as well as patients' status of fatigue, depression, and anxiety, were prospectively collected using various questionnaires one month prior to the scheduled appointment for NPAs at 10-year follow-up. Premorbid education level was collected, and higher education was predefined as more than or equal to 12 years of education and lower education was defined as less than or between 9 and 12 years of education. Employment status prior to stroke and at one year and ten years after stroke was also collected [20] (Figure 2). The questionnaires used in the study are described in detail below.

The Fatigue Assessment Scale (FAS) is a self-report questionnaire used to identify symptoms of chronic fatigue [23] affecting a patient's daily activity. It consists of 10 questions addressing both physical and mental problems associated with fatigue and has a maximum score of 50 points, with higher scores indicating greater degrees of fatigue. The cutoff for post-stroke fatigue was set at 24 points [24]: scores of 24 and higher indicated that the patient had fatigue.

Depression was assessed with the Beck Depression Inventory-II (BDI-II) [25], a self-rating scale that measures depression in adults and adolescents. The test contains 21 questions, each of which is answered with a single score on a 0–3 scale. Higher total scores indicate more severe depressive symptoms. The standardized cutoffs of the BDI-II are ≤13 for minimal depression, 14–19 for mild depression, 20–28 for moderate depression, and 29–63 for severe depression.

Anxiety was assessed with the Beck Anxiety Inventory (BAI) [26], a 21-item multiple-choice self-report assessment. Each answer is given as a score describing how much the patient has suffered from a particular symptom, with the scale ranging from 0 (not at all) to 3 (severely). Higher total scores indicate more severe anxiety symptoms. The standardized cutoffs are ≤7 for minimal anxiety, 8–15 for mild anxiety, 16–25 for moderate anxiety, and 26–63 for severe anxiety.

The simplified modified Rankin Scale questionnaire (mRS) is a standardized, practical, and validated questionnaire for the reliable assessment of a person's functional and disability status [27, 28]. The assessed patient answers five questions with either 'yes' or 'no'; by following their answers on the associated decision tree–like flowchart, a value on a scale from 0 (no symptoms) to 5 (total physical dependence) is arrived at. Scores of 2 or less are considered to indicate total independence [28].

Cognitive function assessments

To assess general cognitive functioning, the Mini-Mental State Examination (MMSE) was carried out for each patient immediately prior to administering the NPA. The MMSE was used at the 7-month post-stroke assessment as a clinical routine more than 10 years prior to the current study (Figure 2). Although it has limitations [29] and the total score of the Wechsler Adult Intelligence Scale (WAIS) can be used as a global cognitive composite score, we chose to use the MMSE because it is considered the gold standard for assessment of global cognitive function.

Domain-specific cognition was assessed by NPA thrice, at one week, seven months, and ten years after stroke (Figure 2). NPA data collected at one week and seven months after stroke onset were retrospectively gathered from the medical records. Working memory and visuospatial function were assessed with the Digit Span and Block Design subtests from the WAIS, respectively. The reasons for the initial NPA at the earlier time points were unknown to us. However, the assessments were performed for clinical reasons and may have been determined by the patients' ability to be assessed and access to a psychologist at that time.

NPAs were often carried out within one week after stroke debut. Some of the participants were assessed again at approximately 7 months (IQR 2–10) after stroke. Four assessors who were blinded to the results of the assessments that had been performed 10 years ago were involved in the study. The full test battery took approximately 2–3 hours, with a 30-minute break and refreshments in the middle of the assessment. To ensure comparability, the tests administered at the 10-year follow-up were selected based on the tests that had been used at the initial assessment in the year of the stroke. It should be noted that the revised WAIS (WAIS-R) and WAIS-III were replaced by the WAIS-IV at the 10-year follow-up. This is because the previous version of WAIS was no longer available to us. Previous validation studies have shown that the WAIS-IV follows the same structure as both the WAIS-III and WAIS-R [30], with a very high correlation between subscales (r = .82–94) [31]. Swedish norms for the WAIS-IV were used as a control [31].

Changes in cognitive functions over the 10 years after a stroke have previously been presented in detail [20]. The following cognitive domains that were found to show significant improvement in our previous study were selected for analysis in the current study: visuospatial function (as measured by the Block Design subtest of the WAIS), working memory (measured using the Digit Span subtest of the WAIS), and general cognitive functioning (measured via the MMSE).

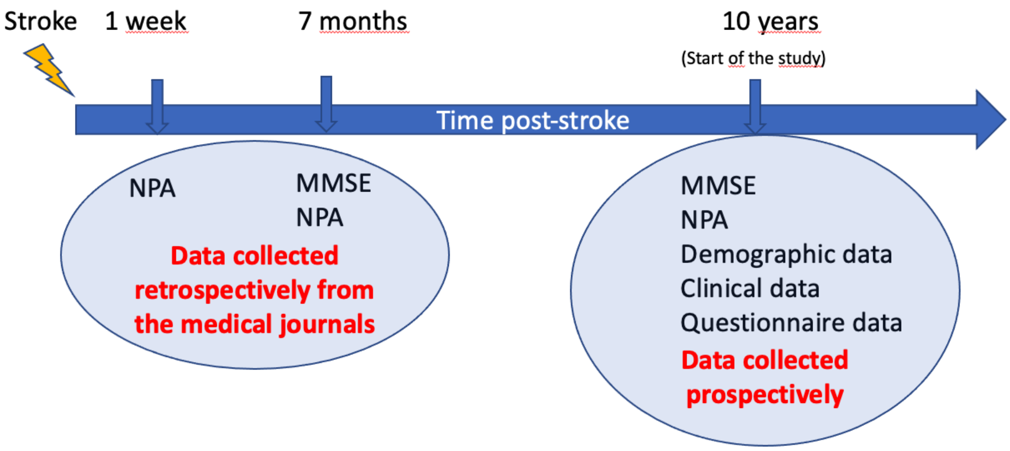

***Figure 2**: Study design and process. Data from neuropsychological assessment (NPA) and Mini-Mental State Examination (MMSE) at approximately 1 week and 7 months after stroke onset were retrospectively collected from the patients' medical records. The clinical data, premorbid education level, and employment, as well as patients' status of fatigue, depression, and anxiety, were prospectively collected using various questionnaires one month prior to the scheduled appointment for MMSE and NPA at 10-year follow-up.*

Data presentation and statistical analysis

Demographic characteristics and NPA data are presented as mean (SD), number and percentage of cases (%), range, or median (25%–75% interquartile ranges [IQR]), as appropriate. No adjustment was made for missing values. A mixed linear model was used as a hierarchical linear model in SPSS to analyze the cognitive differences over time. Each p-value in the post hoc analyses was adjusted to account for multiple comparisons with Bonferroni correction.

Multivariate linear regression with a stepwise method was used to investigate whether the length of education, employment status before and after stroke, stroke subtype, demographic data, and clinical variables could significantly predict improvement in the three cognitive functions assessed at 10-year follow-up: general cognitive functioning, visuospatial function, and working memory. The independent variables included in the model were age, gender, residential status (i.e., whether an individual lived alone), premorbid education, employment prior to stroke onset, employment at one year and ten years after stroke, stroke subtype, functional status, general cognitive functioning at one-week follow-up, visuospatial function at one-week follow-up, and working memory at one-week follow-up. Employment was coded as 1 = full-time job, 2 = part-time job, 3 = sick leave, and 4 = retired; stroke subtype was coded as 1 = ischemic stroke and 2 = hemorrhagic stroke; and length of education was coded as 1 = 9 years, 2 = 12 years, and 3 = >12 years.

Values for tolerance and variance inflation factor (VIF) were calculated to assess the presence of collinearity. Standardized coefficients were used to determine the strength of each independent variable's correlation with improved cognitive function. R2 was examined to determine how much variation in the cognitive functions could be explained by the modeled variables. Linearity and homoscedasticity were examined with Fred's super scatterplot. Independence of errors was tested with the Durbin–Watson test. Normal distribution of the data was assessed with a normal P–P plot.

The software package IBM Statistical Package for the Social Sciences (SPSS) Statistics version 28.0 (SPSS, Chicago, IL, USA) was used to perform the multivariate linear regressions. Figure 2 was generated using GraphPad Prism 9 (San Diego, CA, USA). P-values < 0.05 were considered to indicate statistical significance.

Results

Basic demographic and clinical characteristics

Table 1 presents the baseline demographic and clinical characteristics of the 38 participants. The participants' mean age was 53.9 years (SD 9.1) at stroke onset. All participants were living in the community, and nearly half (n = 18, 47%) had more than 12 years of education. The dominant stroke subtype was ischemia (79%). At 10-year follow-up, participants' mean age was 63.8 years (SD 10.6). Participants exhibited good independence in daily activities at this time, with a median score of 1 on the mRS.

Employment status was collected at three time points. Thirty-three (87%) participants had a full-time or part-time job prior to stroke onset. One year after stroke, 16 (43%) participants had returned to either full-time or part-time work. Almost one third of the participants were employed full- or part-time; another two third were either retired or unemployed. Fatigue was a prevalent problem 10 years after the time of stroke: nearly three-quarters of the participants suffered from fatigue (FAS ≥ 24), with a median score of 25 and a 25%–75% IQR of 21–27. Fewer than one-third of the participants (n = 12) were depressed (BDI-II score > 13), but the median score was 9, with a 25%–75% IQR of 4–14 for the entire group. Approximately one-third (n = 13) had anxiety (BAI score > 8); however, the group's median score of 6 (25%–75% IQR of 2–11) was relatively low. Although information on fatigue, depression, and anxiety was collected at the 10-year follow-up, it provided no predictive value on cognitive function recovery.

Patient Characteristics at stroke onset (n = 38)	
Age [mean (SD)]	54.2 (10.1)
Number of patients (age <30)	3
Number of patients (age between 30-60)	11
Number of patients (age >60)	24
Gender (Men/Women)	19/19
Residential status (live alone/live with somebody/unknown)	7/30/1
Stroke subtype (Ischemia/Hemorrhage/Unknown)	30 /6/2
Education [number of cases (%)]	
Lower education (9–12 years)	19 (50%)
Higher education (> 12 years)	18 (47%)
Unknown	1 (3%)
Employment [number of cases (%)]	
Full-time job	29 (76%)
Part-time job	4 (11%)
Retired/Unemployed	5 (13%)
Employment at 1 year after stroke [number of cases (%)]	
Full-time job	12 (32%)
Part-time job	4 (11%)
Retired/Unemployed	18 (47%)
Unknown	4 (11%)
Characteristics at 10-year follow-up	
Age [mean (SD)]	63.8 (10.6)
Years between stroke onset and follow-up [mean (SD)]	10.5 (0.9)
mRS [Median (25%-75% IQR)]	1 (0-2)
Fatigue assessment score [Median (25%-75% IQR)]	25 (21-27)
BDI-II [Median (25%-75% IQR)]	9 (4-14)
BAI [Median (25%-75% IQR)]	6 (2-11)
Employment [number of cases (%)]	
Full-time job	4 (11%)
Part-time job	6 (16%)
Retired/Unemployed	27 (71%)
Unknown	1 (3%)

Abbreviations: standard deviation (SD); modified Rankin Scale (mRS); interquartile range (IQR); Beck Depression Inventory-II (BDI-II); Beck Anxiety Inventory (BAI)

***Table 1:** Demographic and clinical characteristics of all participants*

Improved cognition

Mean (SD), range, or median (25%–75% IQR) are provided (Table 2) to present the detailed raw data on the cognitive improvements; notably, these cognitive improvements were previously reported in a 2019 study by Elgh and Hu [20]. At 10-year follow-up, the entire group collectively demonstrated a weak but significant improvement in general cognitive functioning as assessed by MMSE compared to the results at 7-month follow-up (from 27 to 29 points, $p = 0.02$). No significant difference was observed when comparing the MMSE scores between the subgroup with a higher independence level (mRS 0–1) and the subgroup with a lower independence level (mRS 2–3).

Median visuospatial function at both 7 months post-stroke and the 10-year follow-up (Table 2) was significantly improved compared to the results at 1 week after stroke ($p = 0.001$ and $p = 0.007$, respectively). However, there was no significant difference between visuospatial function at 7 months and at 10 years after stroke. A median total Digit Span raw score of 17 (25%–75% IQR of 14–19) signaled significant improvements in working memory at 10-year follow-up in comparison with the results at 1 week and 7 months post-stroke ($p < 0.0001$). There were no significant differences in cognitive processing speed or executive function between the follow-up time points

Domain	**Assessment**	**1 week after stroke Raw score**				**7 months after stroke Raw score**				**10 years after stroke Raw score**			
		Mean (SD)	Range	Median (25%-75% IQR)	N	Mean (SD)	Range	Median (25%-75%IQR)	N	Mean (SD)	Range	Median (25%-75%IQR)	N
General cognitive functioning	MMSE	-				27 (3)	11	27 (25-29)	27	28 (2)	8	29 (27-30) †	38
Visuospatial function	WAIS-Block Design	25 (12)	40	27 (15-35)	27	41 (12)	48	39 (34-51) *	19	36 (12)	53	36 (29-48)*	38
Working memory	WAIS-Digit Span (F + B)	12 (4)	19	12 (11-14)	29	15 (5)	18	13 (11-18)	26	16 (3)	13	17 (14-19)*†	38

* Indicates significant difference vs. the data at 1 week after stroke. † Indicates significant difference vs. the data at 7 months after stroke. SD: standard deviation; IQR: interquartile range; MMSE: Mini-Mental State Examination; WAIS: Wechsler Adult Intelligence Scale; F: Forward; B: Backward.

Table 2: *Scores of neuropsychological assessments over 10-year follow-up after stroke onset*

Predictors of cognitive functional recovery

Most of the variables, including age, gender, residential status, employment after stroke, and functional status (mRS score), did not demonstrate any significant predictive value for cognitive recovery.

However, employment prior to stroke, stroke subtype, and length of premorbid education were significant predictors of general cognition, as assessed by MMSE, at 10-year follow-up. A significant regression equation was found [$F(3,15) = 16.95$, $p < 0.001$], with an R^2 of 0.77. Participants' predicted general cognition at 10-year follow-up was equal to 30.15 - 1.09 (employment) -1.77 (stroke subtype) + 0.85 (education). This indicated that participants' general cognition was 1.09 raw scores lower for participants who were unemployed prior to stroke and 1.77 raw scores lower for participants who suffered a hemorrhagic stroke, but 0.85 raw scores higher for participants with more years of education (Table 3A). Working memory (Digit Span score) at 1 week after stroke was a significant predictor of working memory 10 years after stroke. A significant regression equation was found [$F(1,17) = 11.64$, $p = 0.003$], with an R^2 of 0.41. Participants' predicted working memory at 10-year follow-up was equal to 9.14 + 0.55*x ("x" refer to the score on the Digit Span test at 1 week after stroke) – that is, participants' working memory at 10-year follow-up was 0.55 raw scores higher for each Digit Span score received at 1 week after stroke (Table 3B).

Visuospatial function (WAIS-Block Design) at 1 week after stroke was a significant predictor of visuospatial function 10 years after stroke. A significant regression equation was found [$F(1,15) = 19.12$, $p < 0.001$], with an R^2 of 0.56. Participants' predicted visuospatial function at 10-year follow-up was equal to 19.12 + 0.66 *y ("y" refer to the score on WAIS-Block Design test at 1 week after stroke) – that is, participants' visuospatial function at 10-year follow-up was 0.66 raw scores higher for each Block Design score received at 1 week after stroke (Table 3C).

A. Dependent Variable: MMSE score at 10-year follow-up (General cognition)

Variable	Coefficient	Standard Error	t-Statistic	p-value
Employment prior stroke	-1.09	0.22	-0.89	<0.001
Stroke subtype	-1.77	0.60	-0.30	0.009
Length of education	0.85	0.40	2.16	0.048

Constant: 30.15
R-squared: 0.77 Adjusted R-squared: 0.73
Standard Error of the Estimation: 1.25 Durbin–Watson: 1.71

B. Dependent Variable: Total Digital Span score at 10-year follow-up (Working memory)

Variable	Coefficient	Standard Error	t-Statistic	p-value
Total Digital Span score at 1 week after stroke	0.55	0.16	3.41	0.003

Constant: 9.14
R-squared: 0.41 Adjusted R-squared: 0.37
Standard Error of the Estimation: 2.20 Durbin–Watson: 2.87

C. Dependent Variable: Total Block Design score at 10-year follow-up (Visuospatial function)

Variable	Coefficient	Standard Error	t-Statistic	p-value
Total Block Design score <0.001 at 1 week after stroke	0.66	0.15	4.37	

Constant: 19.12
R-squared: 0.56 Adjusted R-squared: 0.53
Standard Error of the Estimation: 6.65 Durbin–Watson: 2.60

Table 3: *Results of multiple linear regression*

Discussion

In the current study, we evaluated whether years of education, employment status before and after stroke, stroke subtype, and various demographic characteristics had any correlation with cognitive recoveries among 38 middle-aged stroke survivors whose cognitive functions had improved 10 years after stroke onset. The primary finding in the current study was that having a full-time job prior to stroke, having an ischemic (as opposed to hemorrhagic) stroke, and having ≥ 12 years of education predicted significantly superior general cognitive function 10 years after a stroke. In addition, working memory and visuospatial function at 1 week after stroke were significantly correlated with their respective functions at 10 years after stroke.

Premorbid employment status was found to be the strongest predictor for better general cognitive recovery, with an MMSE score 1.09 higher for participants with a job before stroke onset in the current study. This is consistent with a recent finding in the KOSCO study, in which occupation was demonstrated to be one of the important buffers against cognitive impairment and found to promote rapid cognitive recovery after stroke [10]. Meanwhile, the participants had good independence in their daily lives based on the lower mRS score demonstrated at 10-year follow-up in the study. However, this late higher independence in daily life was not statistically significantly correlated with the improvement in general cognition in this cohort. These current data suggest that having a job prior to stroke may provide a more advanced challenge in daily life that enhances neuroplasticity and cognitive reserve, which has been demonstrated in individuals with Alzheimer's disease [32, 33]. However, employment status 1 and 10 years after stroke onset did not show any predictive value on the improvement in general cognition in this cohort. This may partly be explained by the fact that we collected only employment status (full-time/part-time/no job) without collecting details on the level/complexity of the job, as well as the small sample size in the current study [10]. Nonetheless, our data suggest that having a job prior to stroke is beneficial for general cognitive recovery after stroke.

Having received more than 12 years of education prior to stroke was another significant predictor of general cognitive improvement, which is consistent with our finding that the mean MMSE score among the participants who received exactly 9 years of education was significantly lower than the score for participants with university education. This outcome is in line with recent findings that high levels of education, as a protective factor against cognitive decline, also promote rapid cognitive recovery after stroke [10, 34]. The effects of education on cognitive improvements after stroke might be explained by the concept of cognitive reserve [12-14], which is defined as the cumulative brain capacity to mitigate cognitive decline due to various brain pathologies, such as stroke, aging, or age-related disease [14, 35]. It is believed that superior cognitive capacity among more highly educated individuals may confer more complex architecture of neuronal networks and an enhanced ability to effectively recruit these networks [14]. This, in turn, may produce better preconditions for activity-derived neuroplasticity after the brain has been damaged, such as in the case of a stroke. Meanwhile, higher education is also associated with better lifestyle choices, better socioeconomic status, less stress, etc., which may influence cognitive function [36]. Consistent with our finding is the association between low education and higher prevalence of cognitive impairment and the development of dementia after a stroke [1, 37]. Thus, together with premorbid employment, premorbid education appears to be one of the best preventive measures for preserving cognitive function in persons with stroke [9, 11, 38]. Moreover, the results of the present study suggest that higher levels of education might be important for cognitive recovery after stroke.

In this cohort, having an ischemic (as opposed to a hemorrhagic) stroke predicted better improvements in general cognition. This is substantiated by findings that hemorrhagic stroke is more strongly associated with cognitive impairment and the development of dementia [16, 39, 40]; however, this was not observed in all studies [15]. However, it remains largely unknown why ischemic and not hemorrhagic stroke is associated with superior general cognitive function. One possible explanation is that hemorrhage may lead to more diffused damage due to widespread intracranial pressure effects and underlying cerebral amyloid angiopathy [16, 39]. It has also been suggested that the difference is attributable to persistent (continuous) underlying cognitive impairment that is induced by the hemorrhagic stroke itself [16].

However, these significant predictors for general cognitive recovery did not predict the improvements in working memory and visuospatial function at 10-year follow-up. Instead, working memory and visuospatial function at 1 week after stroke significantly predicted their respective functions at 10 years after stroke. The reason for these discrepancies in the predictors for general cognitive function and domain-specific functions remains largely unknown. However, it is not difficult to understand why domain-specific functions at the acute stage after stroke may be associated with their respective functions at the chronic stage [41].

This study has several unique strengths. Cognition was assessed at the acute, sub-acute, and chronic phases over a 10-year period after stroke onset, which allowed us to investigate the long-term trajectory of cognitive alterations over the decade after stroke. Moreover, both general and domain-specific outcomes were assessed in this cohort. Although most of the sociodemographic variables, including age, gender, and residential status, did not show any predictive effect on cognitive improvement in the study, our data provide a distinct opportunity to enhance our understanding of the mechanisms of cognitive recovery after stroke.

Our study has some methodological biases, the first of which is that stroke location and stroke severity at onset – factors that can affect the degree of cognitive impairment [42] – were not collected in the study. Another challenge is that different versions of the WAIS cognitive battery were used: at the time of first assessment, participants were tested with the WAIS-III, whereas WAIS-IV was used at the 10-year mark due to the loss of access to WAIS-III. Though studies have shown that the two versions are closely correlated and measure the same constructs, the possibility that the difference in tests could have affected the results should not be discounted. An additional limitation concerns the length and nature of the study, which was longitudinal and took place over a full decade. One of the major methodological problems affecting longitudinal studies is attrition, which can deteriorate the generalizability of findings if participants who stay in a study differ meaningfully from those who drop out. Of the 102 middle-aged first-ever stroke patients with acute NPAs who were recruited for the study, only 38 were both qualified and willing to participate in the 10-year follow-up. We recognize that these 38 participants are not fully representative of patients in the literature on long-term cognitive recovery post-stroke [1-4]. The results are therefore not generalizable to the entire population of middle-aged stroke survivors; moreover, the small sample size confers limited statistical power. Nonetheless, our results demonstrated that premorbid employment and higher education may have played important roles in the patients who were able to ameliorate their post-stroke cognitive dysfunctions, although the mechanisms governing these recoveries are not yet fully understood.

Conclusions

We found that having a job prior to stroke, suffering from an ischemic rather than a hemorrhagic stroke, and having obtained higher levels of education were strong predictors of high levels of general cognitive functioning 10 years after stroke onset among 38 middle-aged individuals. Our data provided some hypotheses; namely, that premorbid employment and higher education as well as having an ischemic stroke might be crucial for post-stroke cognitive recovery. A large-scale study is necessary to confirm the veracity and generalizability of these findings.

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Declaration of interest statement

The authors report there are no competing interests to declare.

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