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## **The impact of bilingualism on cognitive outcome after stroke**

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TABLE 1. Clinical characteristics and cognitive outcomes of monolinguals and bilinguals

TABLE 2. Factors predicting post-stroke cognitive impairment in the binary logistic regression model

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## Abstract

**Background and purpose:** Bilingualism has been associated with slower cognitive ageing and a later onset of dementia. In this study, we aimed to determine whether bilingualism also influences cognitive outcome after stroke.

**Methods:** We examined 608 ischemic stroke patients from a large stroke registry and studied the role of bilingualism in predicting post-stroke cognitive impairment in the absence of dementia.

**Results:** A larger proportion of bilinguals had normal cognition compared to monolinguals (40.5 % vs 19.6 %,  $P < 0.0001$ ) while the reverse was noted in patients with cognitive impairment, including vascular dementia and vascular mild cognitive impairment (monolinguals 77.7% vs bilinguals 49.0%,  $P < 0.0009$ ). There were no differences in the frequency of aphasia (monolinguals 11.8% vs bilinguals 10.5%,  $P = 0.354$ ). Bilingualism was found to be an independent predictor of post-stroke cognitive impairment.

**Conclusions:** Our results suggest that bilingualism leads to a better cognitive outcome following stroke, possibly by enhancing cognitive reserve.

## **Introduction**

Given the social burden of cognitive impairment due to cerebrovascular disease,<sup>1</sup> several studies have identified factors that influence cognitive outcome after stroke.<sup>2</sup> A potential protective factor not yet examined in this context is bilingualism. Recent research suggests that bilingualism is associated with better cognitive function in ageing,<sup>3</sup> and a later onset of dementia, including vascular dementia (VaD).<sup>4</sup> These findings are interpreted in the context of an advantage in executive control and enhanced cognitive reserve in bilinguals.<sup>5</sup> However this effect is confounded by immigration and education, and continues to be debated.<sup>6</sup> To explore this further, we studied the association between bilingualism and cognitive outcome of stroke. We hypothesised that if bilinguals differ from monolinguals in vascular risk factor profile, they would present with a later occurrence of stroke. In contrast, if bilinguals have indeed a better cognitive reserve, we would expect in them the same age of stroke but a more favourable cognitive outcome. Nizam's Institute of Medical Sciences (NIMS), Hyderabad is a clinical research centre well suited to explore this relationship. Stroke and dementia patients are assessed by the same team.<sup>7,8</sup> Bilingualism is common, without the confounding effect of immigration, and has been systematically studied.<sup>4</sup>

## **Methods**

### **Patients**

The patients were participants in the NIMS stroke registry, initiated to study clinical profile and outcome in consecutive cases of acute stroke.<sup>7</sup> Records of patients evaluated during 2006-2013 were reviewed. Ischemic stroke patients >18 years and evaluated 3-24 months after stroke, were included.

Patients with disabling stroke (modified Rankin Scale $>4$ ), severe comorbidities, inadequate data and pre-existing dementia were excluded. The NIMS ethics committee approved the study.

### **Clinical evaluation**

All patients were evaluated with a detailed history and clinical evaluation by experienced behavioural neurologists, stroke specialists (SA, SK, RK) and trained psychologists using a structured diagnostic protocol adapted from the Cambridge Memory Clinic model.<sup>9</sup> Cognitive evaluation was done using Addenbrooke's Cognitive Examination-revised (ACE-R), a multidimensional cognitive screening tool, adapted for Telugu and Hindi speaking populations in Hyderabad. ACE-R has been validated in large studies of stroke outcome.<sup>10</sup> Clinical Dementia Rating (CDR) scale was used to assess severity of dementia. All patients underwent brain imaging (CT scan and/or MRI). Bilingualism was defined as the ability to communicate in two or more languages in interaction with other speakers of these same languages.<sup>4</sup>

### **Definition of outcome variables**

All stroke patients were classified into the following diagnostic groups: VaD, vascular mild cognitive impairment (VaMCI), aphasia and strokes with normal cognition. VaD was diagnosed as fulfilling NINDS-AIREN criteria for possible or probable VaD.<sup>11</sup> VaMCI was diagnosed in subjects with impairment in at least one cognitive domain sub-score of ACE-R ie. attention, memory, fluency, language and visuospatial domains and absence of dementia on clinical interview or Clinical Dementia Rating scale (CDR). Impairment in a cognitive domain was defined if the score on the ACE-R subdomain was less than 2.00 SD below the mean level of age- and education-matched norms. Patients with VaMCI and VaD were considered to have post stroke cognitive impairment. Diagnosis of aphasia was made by two

experienced behavioural neurologists (SA and SK) and trained psychologists by obtaining a detailed history for language deficits, and assessment of language through a clinical interview supported by language sub-scores of ACE-R. Normal cognitive performance was defined as the absence of impairment on any one of the cognitive domain sub-scores of Addenbrooke's Cognitive Examination- Revised based on age and education matched norms. Please refer to the supplemental methods and tables I and II for details of ACE-R adaptation and normative data in local languages (<http://stroke.ahajournals.org>).

### **Statistical analysis**

Clinical profiles of monolingual and bilingual subjects were compared using independent samples *t* test for continuous variables and chi-square test for categorical variables. Series of binary logistic regressions were conducted to investigate the effect of relevant variables (enter method in SPSS). Presence of cognitive impairment was the fixed factor for the logistic regression. Statistical analysis was performed using SPSS 20.0 for windows software (SPSS Inc., Chicago, IL) and significance was set at  $P < 0.05$ . Bonferroni adjusted *p* values were followed to correct for multiple testing issues.

### **Results**

Of the 608 patients, VaD was diagnosed in 189 (31.1%), VaMCI in 159 (26.2%), aphasia in 67 (11.0%); 193 (31.7%) were found to be normal. On comparing for post-stroke cognitive outcomes, a larger proportion of bilinguals had normal cognition while the reverse was noted in the stroke patients with cognitive impairment (Table 1). There were no differences in the outcome of aphasia between monolinguals and bilinguals. On excluding aphasics, bilinguals had higher scores on total ACE-R and across attention, fluency and visuospatial domains, but not on memory and language (Supplemental table-III, <http://stroke.ahajournals.org>).

To determine factors associated with post-stroke cognitive impairment, we compared patients with normal (n=193, 35.7%) and impaired cognition (n=348, 64.3%). Older age, lower educational and occupational status, monolingualism, and vascular risk factors were significant ( $P<0.003$ ) following Bonferroni correction for multiple testing). To study whether bilingualism was independently associated with post-stroke cognitive impairment, we performed a series of logistic regressions. There was no collinearity effect among the factors. The first logistic regression incorporated demographic variables, the second included stroke-related variables and the third examined risk factors. Significant variables from the analyses were entered into a final logistic regression analysis. Following a Bonferroni correction, bilingualism and age, were found to be significant independent predictors (Table 2).

## **Discussion**

This is the first study examining systematically the relationship between bilingualism and cognitive outcome after stroke. The percentage of patients with intact cognitive functions post-stroke was more than twice as high in bilinguals than in monolinguals. In contrast, patients with cognitive impairment were more common in monolinguals. In addition to other well established factors,<sup>2</sup> bilingualism emerged as an independent predictor of post-stroke cognitive impairment. Furthermore, no differences were found between bilinguals and monolinguals in vascular risk factors or in the age at stroke, suggesting that the observed differences are not due to a healthier lifestyle among bilinguals.

The only outcome not influenced by bilingualism was the frequency of aphasia. Although this might look surprising at the first sight, this finding is in line with current research suggesting that the mechanism underlying the protective effect of bilingualism is due not to better linguistic but executive functions acquired through a lifelong practice of language switching.<sup>6</sup>



The higher scores of bilinguals on attention and fluency domains, with no difference in language sub-score, support this hypothesis. To conclude, our results suggest that bilingualism has a protective effect against the development of post-stroke cognitive impairment.

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### **Conflicts of Interest**

None

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**Table legends:**

TABLE 1. Clinical characteristics and cognitive outcomes of monolinguals and bilinguals

TABLE 2. Factors predicting post-stroke cognitive impairment, in the binary logistic regression model

**TABLE 1. Clinical characteristics and cognitive outcomes of monolinguals and bilinguals**

	Monolinguals (n=255,41.9%)	Bilinguals (n=353,58.1%)	<i>P</i>
Sociodemographic factors			
Age at examination (mean) (SD, range)	56.6 (12.2)(25-89)	57.0 (12.7)(25-92)	0.661
Age at stroke (mean) (SD, range)	56.0 (12.3)(23-88.7)	56.5 (12.7)(23-91.7)	0.639
Males	170(66.7%)	308(87.3%)	<0.0001 <sup>b</sup>
Literates	164(64.3%)	328(92.9%)	<0.0001 <sup>b</sup>
Occupation <sup>*</sup>			
Elementary	12(8%)	3(1%)	
Skilled	128 (85.3%)	195(67.2%)	<0.0001 <sup>b</sup>
Associate professionals	7(4.7%)	56(19.3%)	
Professionals	3(2%)	36(12.4%)	
Vascular risk factors			
Hypertension	164(64.3%)	216(61.2%)	0.242
Diabetes	91(35.7%)	126(35.7%)	0.534
Cardiac disease	34(13.3%)	63(17.8%)	0.082
Smoking <sup>‡</sup>	55(22.8%)	84(25.0%)	0.308
Chronic alcoholism	63(26.1%)	84(25.0%)	0.415
Stroke characteristics			
Duration after stroke (months)	7.2(6.5)(3-24)	6.8(6.5)(3-24)	0.467
Laterality of infarct <sup>‡</sup>			
Right	62(26.7%)	73(23.2%)	
Left	86(37.1%)	99(31.6%)	0.116
Bilateral	84(36.2%)	141(45.0%)	
Location of infarct			
Cortical	34(13.3%)	64(18.1%)	
Subcortical	162(63.5%)	215(60.9%)	0.120
Cortical-subcortical	45(17.6 %)	44(12.5%)	
Brainstem/cerebellum	14(5.5%)	30(8.5%)	
Modified Rankin Scale			
Mild disability (0-2)	191(74.9%)	256(72.5%)	0.262
Moderate to severe (3-4)	64(25.1%)	97(27.4%)	

Prior stroke	35(13.7%)	51(14.4%)	0.448
Family history of dementia <sup>§</sup>	5(2.1%)	12(3.6%)	0.222
Cognitive outcome			
Normal	50(19.6%)	143(40.5%)	<0.0001 <sup>b</sup>
Cognitive impairment (VaMCI + VaD)	175 (77.7%)	173 (49.0%)	0.0009 <sup>b</sup>
Aphasia	30(11.8%)	37(10.5%)	0.354

\*missing data n=67 (housewives n=101 excluded)

†missing data n=85

‡ missing data n=63

§ missing data n=46

Following Bonferroni correction for 20 multiple regression tests, p , 0.0025 was considered a significant P value

**TABLE 2. Factors predicting post-stroke cognitive impairment in the logistic regression model**

Factor	<i>P</i>	OR Estimate (95% CI)
Demographic variables		
Age	<0.0001	1.032(1.015-1.050) <sup>b</sup>
Bilingualism	0.001	2.184(1.379-3.458) <sup>b</sup>
Gender	0.977	0.986(0.373-2.607)
Education	0.225	1.496(0.781-2.865)
Occupation	0.881	1.085(0.369-3.190)
Stroke-related variables		
Left-sided infarcts	0.051	1.511(0.990-2.304)
Prior stroke	0.030	0.526(0.295-0.939)
Infarct location	0.199	1.532(0.799-2.939)
Duration after stroke	0.058	0.974(0.949-1.001)
Risk factors		
Hypertension	0.014	0.621(0.424-0.909) <sup>b</sup>
Chronic alcoholism	0.434	0.815(0.489-1.360)
Smoking	0.151	0.680(0.402-1.151)
Cardiac disease	0.787	0.932(0.560-1.552)
Diabetes	0.110	0.722(0.485-1.076)
Family history of dementia	0.063	0.141(0.018-1.109)
Final regression model		
Bilingualism	<0.001	3.007 (2.032-4.452) <sup>b</sup>
Age	<0.001	1.026(1.007-1.039) <sup>b</sup>
Hypertension	0.056	0.673(0.457-0.991)

Abbreviations: OR= odds-ratio; CI=confidence interval

Following Bonferroni correction for 3 multiple regression tests,  $p < 0.017$  was considered a significant P value