Neuropsychological Profiles of 5-Year Ischemic Stroke Survivors by Oxfordshire Stroke Classification and Hemisphere of Lesion

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Background and Purpose—Although the neuropsychological literature typically examines stroke outcomes by hemisphere of lesion, the medical literature provides classifications more closely linked to circulatory distribution impacted by stroke. This article examined profiles of cognitive function by hemisphere and by Oxfordshire Community Stroke Project stroke classification.

Methods—This study included a sample of 315 5-year ischemic stroke survivors. Assessment included tests of verbal memory, visual memory, word finding/verbal fluency, abstract visual reasoning, executive functioning, and speed of processing.

Results—The sample produced scores within 1 standard deviation of the normative mean on tests of abstract visual reasoning, verbal memory, and visual recall. Impaired performances were observed for executive function and processing speed. Profile analysis revealed no significant differences in overall cognitive performance or in the profile of performance across measures by hemisphere of lesion. However, groups defined by Oxfordshire Community Stroke Project categories produced significantly different cognitive profiles. Post hoc analyses indicate those with posterior stroke performed best overall on all tests except the Stroop Dots trial, whereas those with total anterior stroke produced significantly worse scores on tasks requiring visual abstract reasoning (Block Design, Rey Figure Copy), word finding (Boston Naming Test), and processing speed (Stroop Dots, Trails A).

Conclusions—Oxfordshire Community Stroke Project stroke subtypes identified significant differences between groups, suggesting this classification system is of greater use than hemisphere of lesion in predicting poststroke cognitive outcomes. (Stroke. 2012;43:50-55.)

Key Words: classification ■ hemisphere ■ ischemic stroke ■ neuropsychological assessment ■ profile

In addition to the physical consequences of stroke, cognitive impairments occur in nearly half of stroke survivors.1,2 These impairments are associated with greater mortality and disability,3 they may occur after mild to moderate stroke,4 and they may be more important determinants of functional outcomes after stroke than physical disability.3,5,6

Stroke can be classified into 2 general types: ischemic and hemorrhagic. Ischemic stroke, the focus of this article, which accounts for 80% of strokes, refers to disruption of the blood supply to the brain resulting in an infarct or area of dead tissue. Classification systems are based on stroke location (eg, hemisphere of lesion) or initial clinical symptoms (eg, Oxford Community Stroke Project [OCSP] classification): total anterior circulation stroke [TACS], lacunar stroke [LACS], partial anterior circulation stroke [PACS], or posterior circulation stroke [POCS]).

In studies examining physical outcomes in relation to stroke subtype, those with ischemic stroke (especially LACS) generally have relatively high short-term and long-term survival rates.8,9 In contrast, TACS are associated with greatest case fatality and poor functional outcomes.4,7,10 Research analyzing outcomes in relation to hemisphere of lesion vary; some studies report that right hemisphere lesions relate to poorer functional outcomes,11,12 whereas others report no relationship.13—15

Interestingly, studies examining cognitive outcomes after stroke have focused almost entirely on hemisphere of lesion. Generally those with left-side lesions show language and

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speech disorders, whereas those with right-side lesions show predominantly perceptual and visuospatial deficits.\textsuperscript{16} Given that the purpose of cognitive assessment is to examine impairments associated with damage to a given brain area, it is surprising that few studies have examined neuropsychological outcomes in relation to OCSP subtypes, because it may inform the provision of targeted rehabilitation.\textsuperscript{17}

This study examined profiles of cognitive performance in 5-year stroke survivors in relation to stroke subtype based on hemisphere of lesion (left, right) and the OCSP classification. In keeping with the neuropsychological literature, it was hypothesized that those with left hemisphere stroke would exhibit more deficits on verbal tests and those with right hemisphere stroke would exhibit deficits on visual tasks. Further, it was hypothesized that those with total anterior stroke would exhibit more executive dysfunction, whereas those with lacunar stroke would exhibit the fewest deficits.

### Materials and Methods

Data were collected as part of the Auckland Stroke Outcomes (ASTRO) study of 5-year stroke outcomes (March 2007–February 2008),\textsuperscript{2,8} which sourced participants and baseline data from the Auckland Regional Community Stroke (ARCOS; 2002–2003) population-based incidence study.\textsuperscript{2,8} The design, method, and primary findings are described elsewhere.\textsuperscript{2,8} In brief, potential participants were all ARCOS participants with ischemic stroke consenting to involvement in future research. Strokes were classified based on neuroimaging findings (92\% had CT/MRI/autopsy verification within days of stroke) and methodology for population-based stroke incidence studies and standard definitions were used.\textsuperscript{19} The ASTRO study received approval from the Northern X Auckland Regional Ethics Committee.

Attempts were made to contact all potential participants (n = 748; Figure 1). Seventy-one potential participants had died and 20 were not located. Of 657 remaining, 239 did not consent. Of 418 who participated, 336 had ischemic stroke, 315 of whom completed some neuropsychological assessments (Figure 1). After gaining verbal informed consent, subjects were interviewed via telephone to complete questionnaires (Barthel Index, Short Form-36; data reported elsewhere\textsuperscript{2,8}) and to organize face-to-face assessments at the participants usual place of residence.

Face-to-face interviews included obtaining written consent, neuropsychological tests, and National Institutes of Health Stroke Scale. Neuropsychological test were commonly used, well-validated tests of: verbal memory, California Verbal Learning Test 2nd edition\textsuperscript{20} (word list learning, recall, recognition) and logical memory\textsuperscript{21} (immediate and delayed story recall); visual memory, Visual Paired Associates\textsuperscript{22} (color–design pair learning; no physical response) and Rey-Osterrieth Complex Figure (visuospatial construction and recall);\textsuperscript{22} language, Boston Naming Test\textsuperscript{23} (anomia) and Controlled Oral Word Association\textsuperscript{23} (verbal fluency); visuospatial functioning, Block Design\textsuperscript{24} (visual reasoning/problem solving; motor speed) and Matrix Reasoning\textsuperscript{25} (reasoning/problem solving; no speed component); and executive function and information processing speed, Trails A/B\textsuperscript{26} (mental flexibility, speed), Stroop\textsuperscript{26} (cognitive speed, set-shifting, inhibition), and Integrated Visual Auditory Continuous Performance Test\textsuperscript{27} (attention, impulsivity, speed; auditory and visual). Face-to-face assessments lasted ~2.5 hours, with similar test batteries well-tolerated 3 months after stroke.\textsuperscript{28} Where required, testing occurred over 2 sessions.

In patients with expressive aphasia, verbal assessments were omitted. If receptive aphasia was suspected, then ability to participate was determined via practice items, with administration proceeding when participants demonstrated understanding of task requirements. Tasks requiring physical responses were omitted when hemiplegia would impact performance. When English was poor, interpreters were used. Tasks requiring visual abilities were not administered when visual difficulties would impact performance.

### Statistical Analyses

Neuropsychological assessments were administered and scored according to standard procedures, with raw scores converted to z scores using age-matched (and, when available, education and gender) normative data.\textsuperscript{29} New Zealand norms were used when available.\textsuperscript{30,31} Consistent with standard definitions, z scores \( < -1 \) were considered below average.

Profile analyses were conducted using PSAW 17.0 to compare neuropsychological outcomes by hemisphere of lesion (ie, left, right) and then by OCSP classification (ie, TACS, LACS, PACS, POCS). Profile analysis is an application of multivariate analysis of variance that provides an indication of overall differences between levels on the linear combination of dependent variables (ie, groups, hemisphere of lesion, or OCSP subtype), the flatness of profiles (ie, are the outcomes similar across the neuropsychological tests?), and parallelism (ie, do different groups have parallel profiles equivalent to an interaction?).\textsuperscript{32} Whereas the classification into OCSP subtypes has resulted in unequal group sizes, PSAW 17.0 provides adjustment for unequal groups. Post hoc analyses used Bonferroni correction.

### Results

**Sample Characteristics**

Demographic and stroke characteristics of the sample are in Table 1. The average age of the sample at stroke onset was 71.24 years, with just more than half being male. Average performance on Barthel Index, National Institutes of Health Stroke Scale, and modified Rankin Scale\textsuperscript{33} suggest a largely independent sample with relatively good outcomes, with 16.5\% meeting criteria on the Hodgkinson Mental Test for
Table 1. Demographic and Baseline Stroke Characteristics of Participants (n=336)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean (SD)</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at stroke</td>
<td>71.24 (12.4)</td>
<td></td>
</tr>
<tr>
<td>Barthel Index</td>
<td>17.84 (4.4)</td>
<td></td>
</tr>
<tr>
<td>NIHSS</td>
<td>4.33 (4.5)</td>
<td></td>
</tr>
<tr>
<td>Gender, N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>179 (53.3%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>157 (46.7%)</td>
<td></td>
</tr>
<tr>
<td>Ethnicity, N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>European</td>
<td>257 (76.5%)</td>
<td></td>
</tr>
<tr>
<td>Maori</td>
<td>18 (5.4%)</td>
<td></td>
</tr>
<tr>
<td>Pacific Island</td>
<td>29 (8.6%)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>28 (8.3%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>4 (1.2%)</td>
<td></td>
</tr>
<tr>
<td>English first language, N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>262 (83.9%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>54 (16.1%)</td>
<td></td>
</tr>
<tr>
<td>Hemisphere of lesion, N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>169 (50.3%)</td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>167 (49.7%)</td>
<td></td>
</tr>
<tr>
<td>Modified Rankin Scale, N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;3</td>
<td>249 (74%)</td>
<td></td>
</tr>
<tr>
<td>≥3</td>
<td>87 (26%)</td>
<td></td>
</tr>
<tr>
<td>Hodgkinson Mental Test</td>
<td>8.44 (3.13)</td>
<td></td>
</tr>
<tr>
<td>N (%) ≥6</td>
<td>50 (16.3%)</td>
<td></td>
</tr>
<tr>
<td>OCSP Classification, N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TACS</td>
<td>54 (16.2%)</td>
<td></td>
</tr>
<tr>
<td>PACS</td>
<td>157 (46.7%)</td>
<td></td>
</tr>
<tr>
<td>LACS</td>
<td>47 (14.0%)</td>
<td></td>
</tr>
<tr>
<td>POCs</td>
<td>77 (22.6%)</td>
<td></td>
</tr>
<tr>
<td>Uncertain</td>
<td>1 (0.6%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 1 indicates that the sample produced scores within 1 standard deviation of the normative mean on tests of abstract functioning. No statistically significant difference in levels was found between groups when scores were averaged across the regions of the brain, indicating that the sample was well-matched in terms of cognitive ability.

Overall Performance
As seen in Table 2, the sample produced scores within 1 standard deviation of the normative mean on tests of abstract functioning. Most participants were European and >83% spoke English as a first language. Similar proportions of the sample had left versus right hemisphere strokes. Using OCSP classifications, >46% of strokes were partial anterior (PACS), whereas just >22% were posterior (POCS), 16% were total anterior (TACS), 14% were lacunar (LACS), and <1% were of uncertain type.

The sample produced scores within 1 standard deviation of the normative mean on tests of abstract, perceptual, and visuoperceptual ability (Block Design, Matrix Reasoning), tests of verbal memory (California Verbal Learning Test 2nd edition, Logical Memory), and on a test of visual memory and learning (Visual Paired Associates). On the remaining visual memory test (Rey-Osterrieth Complex Figure), recall scores were within 1 standard deviation of the normative mean, whereas the copy score, which requires executive function, was >2 standard deviations below the normative mean. Lower performances occurred on tasks requiring executive function (Integrated Visual Auditory Continuous Performance Test, Trails, Stroop). A low score (>1 standard deviation below normative mean) was also produced on a task of naming ability (Boston Naming Test), whereas verbal fluency (Controlled Oral Word Association) decreased to within 1 standard deviation below the normative mean.

Performance by Hemisphere
In preliminary analysis examining differences in cognition by hemisphere found, Mauchles sphericity was significant (W = .00031; χ² (135) = 627.01; P < 0.001), indicating covariance heterogeneity. A profile analysis was performed with hemisphere of stroke (left, right) as the grouping variable and z scores across neuropsychological tests as dependent variables. No statistically significant difference in levels was found between groups when scores were averaged across the domains of abstract, perceptual, and visuoperceptual functioning.
tests (F(16, 68) = 0.788; P = 0.694). Using Wilks criterion, scores deviated significantly from flatness (F(16, 68) = 14.58; P < 0.001), but the profiles did not differ significantly from parallelism (F(15, 68) = 0.73; P = 0.766). This indicates that whereas performance differed significantly between tests administered, this variation was similar between groups.

Performance by OCSP Group

In examining differences in cognition by OCSP categories, Mauchssley sphericity was significant (W = 0.00082; X(135) = 617.63; P < 0.001), indicating covariance heterogeneity. Profile analysis was performed with OCSP category (TACS, LACS, PACS, POCS) as the grouping variable and z scores across cognitive tests as dependent variables. Uncertain strokes were excluded because profile analysis requires the number of participants in the smallest group to exceed the number of dependent variables.32

When levels were tested, there were no significant main effect of OCSP group (F(48, 197) = 0.1.203; P = 0.192). Using Wilks criterion, scores deviated significantly from flatness (F(16,66) = 12.15; P < 0.001) and parallelism (F(48, 197) = 11.11; P = 0.029). Thus, whereas overall mean level of cognitive deficits did not differ between groups, the groups differed in the tests when high and low scores were obtained; that is, the profile of deficits differed (Figure 2).

Post hoc analyses (using Bonferroni correction) show that those surviving TACS produced significantly worse scores on Rey-Osterrieth Complex Figure copy (P = 0.006), Boston Naming Test (P = 0.009), and Block Design (P = 0.010) than those with POCS. Those with POCS produced the best scores across tests, with the exception of the Stroop color name trial. Those with TACS produced significantly worse scores on Trails A than all other stroke subtypes (P = 0.001, 0.030, and 0.026 for POCS, LACS, and PACS, respectively), and also produced a slower Stroop Dots performance than those with LACS or POCS. Those with PACS stroke performed significantly worse than LACS (P = 0.004) or POCS (P = 0.005) on the Stroop Dots trial, but did not differ significantly from TACS. Those with LACS performed significantly worse than those with POCS on Matrix Reasoning (P = 0.010).

Discussion

Five years after ischemic stroke, survivors showed a range of cognitive deficits. Tasks reliant on executive functions and processing speed (Integrated Visual Auditory Continuous Performance Test, Trails, Stroop) were the most impaired. Several other studies report similar outcomes at 3,34 12,35 and 36 months after stroke.36 Whereas the neuropsychological literature often reports poststroke cognition related to hemisphere of lesion, this study suggests that left and right hemisphere strokes do not produce significantly different profiles of performance. In the neuropsychological literature, the general consensus is that those with left-side lesions will show language and speech disorders, whereas those with right-side lesions show predominantly perceptual and visuospatial deficits.16 Recent studies suggest refining lesion location is more predictive of cognitive impairment and recovery.37 In associating outcomes and hemisphere of lesion, findings have varied with reports that right hemisphere lesions relate to poorer functional outcomes poststroke11,12 and in rehabilitation units,38 whereas others report no relationship.13–15 Thus, hemisphere of lesion may not be a good predictor of recovery after stroke.

OCSP stroke subtypes produced significantly different neuropsychological test profiles. TACS survivors had the greatest cognitive impairment, particularly on visual organization/problem solving tasks (Rey-Osterrieth Complex Figure copy, Block Design, Trails A) and word finding (Boston Naming Test). Those with total or partial anterior stroke
(TACS or PACS) produced worse scores on the speeded Stroop Dots test. This is consistent with the literature linking executive abilities required by such tests to frontal lobe functioning, which is implicated by strokes affecting the anterior circulation.

Those with POCs produced the best cognitive profile, obtaining significantly better scores compared to the TACS on several tasks and better scores than those with LACS on Matrix Reasoning, a test of visuoperceptual function and abstract reasoning. Their relatively unimpaired performance is possibly because the posterior vascular system is less definitively linked to language and executive tasks. Poorer performance of those with lacunar stroke may be attributable to disruption of the wider communication networks needed to integrate visuo-perceptual abilities, abstract reasoning, and problem solving. This is consistent with the view that higher mental functions result from complex/integrated communication, with degree of cognitive impairment more related to overall integrity than to a single area of damage.

Only 2 studies have examined cognitive outcomes by OCSP stroke type, both of which used a screening test (Mini-Mental State Examination), which has limited ability to determine cognitive impairment after stroke. In a study of 9-day post-stroke cognition, anterior stroke (TACS and PACS) independently predicted scores on the Mini-Mental State Examination, which is consistent with the present finding. In a study of 3-year stroke outcomes, the relationship between current level of cognitive impairment and stroke type was not examined. The current findings reflect the literature relating OCSP stroke subtypes to other outcomes, with population-based studies and a systematic review reporting that TACS have the worst cognitive profile, those with TACS and PACS are likely to present with more long-term cognitive deficits after stroke. Thus, clinicians should be vigilant in identifying these deficits and providing appropriate interventions. Making more accurate predictions regarding cognitive outcomes would inform the provision of rehabilitation and would provide patients and caregivers with more accurate information regarding cognitive recovery.

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Disclosures

None.

References

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