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Picturing the Size and Site of Stroke With an Expanded National Institutes of Health Stroke Scale

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Background and Purpose—The National Institutes of Health Stroke Scale (NIHSS) includes minimal assessment of cognitive function, particularly in right hemisphere (RH) stroke. Descriptions of the Cookie Theft picture from the NIHSS allow analyses that (1) correlate with aphasia severity and (2) identify communication deficits in RH stroke. We hypothesized that analysis of the picture description contributes valuable information about volume and location of acute stroke.

Methods—We evaluated 67 patients with acute ischemic stroke (34 left hemisphere [LH]; 33 RH) with the NIHSS, analysis of the Cookie Theft picture, and magnetic resonance imaging, compared with 35 sex- and age-matched controls. We evaluated descriptions for total content units (CU), syllables, ratio of left:right CU, CU/minute, and percent interpretive CU, based on previous studies. Lesion volume and percent damage to regions of interest were measured on diffusion-weighted imaging. Multivariable linear regression identified variables associated with infarct volume, independently of NIHSS score, age and sex.

Results—Patients with RH and LH stroke differed from controls, but not from each other, on CU, syllables/CU, and CU/minute. Left:right CU was lower in RH compared with LH stroke. CU, syllables/CU, and NIHSS each correlated with lesion volume in LH and RH stroke. Lesion volume was best accounted by a model that included CU, syllables/CU, NIHSS, left:right CU, percent interpretive CU, and age, in LH and RH stroke. Each discourse variable and NIHSS score were associated with percent damage to different regions of interest, independently of lesion volume and age.

Conclusions—Brief picture description analysis complements NIHSS scores in predicting stroke volume and location. **(*Stroke*. 2016;47:1459-1465. DOI: 10.1161/STROKEAHA.115.012324.)**

Key Words: aphasia ■ cognition disorders ■ linear models ■ magnetic resonance imaging ■ stroke

The National Institutes of Health Stroke Scale (NIHSS) was developed as an impairment scale that could be administered reliably by a variety of clinicians in a relatively short time to evaluate stroke severity before and after treatment, primarily to evaluate the effects of intervention.[1] This 42-point scale includes basic assessments of functions frequently affected by stroke: level of consciousness, extraocular movements, visual fields, facial movement, limb strength, tactile function, coordination, language, motor speech, and spatial attention.[2,3] Intrarater and inter-rater reliability after training in administration is excellent.[4] Despite outstanding strengths and proven usefulness, several studies have provided evidence that the NIHSS does not measure deficits equally in left hemisphere (LH) and right hemisphere (RH) stroke. Studies have consistently found that volume of RH lesions, compared with LH lesions, is underestimated by the NIHSS.[5,6] For example, for each 5-point category of NIHSS scores (eg, 6–10), the median volume of RH infarcts was approximately twice the median volume of LH infarcts.[5] Gottesman et al[7] hypothesized that this discrepancy was because of the fact that NIHSS has few points for RH cognitive functions but several more for language (LH functions). They showed that this bias could be corrected by adding additional points for errors in simple tests of hemispatial neglect. Likewise, a recent study showed that NIHSS scores are related to the location of LH but not RH damage, after controlling for age and sex.[8] Preexisting burden of leukoaraiosis also modulates the relationship between NIHSS scores and infarct volume,[9] and leukoaraiosis burden influences the severity of neglect independently of infarct volume in RH stroke.[10]

Although the NIHSS is responsive to change,[1] 1 study showed that even a single test of neglect was more sensitive

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to change in total volume of ischemic tissue in RH stroke than was the NIHSS.[11] It was argued that the relatively low sensitivity of the NIHSS to change in volume of ischemic tissue in RH stroke might be explained by the fact that it is heavily weighted toward motor function. Therefore, although it assesses a broad range of potential stroke sequelae, supplementing it with tasks that assess both left and right cortical damage (particularly right cortical damage) might improve its effectiveness in measuring stroke severity and estimating volume of stroke.

One component of the NIHSS is a description of the Cookie Theft picture (originally from the Boston Diagnostic Aphasia Examination[12]), which is currently used to rate aphasia severity qualitatively (0–2). However, more quantitative analyses have been shown to be sensitive to mild to severe aphasia[13] and RH cortical dysfunction.[14,15] We hypothesized that quantitative analysis of the Cookie Theft picture, which does not add time to NIHSS administration, contributes valuable information about volume and location of acute infarct, independently of the current NIHSS score.

Methods

Participants

We enrolled 67 participants with acute ischemic hemispheric stroke, 34 LH and 33 RH, and 35 age and sex-matched healthy controls. Patients with stroke were tested (with NIHSS and picture description) within 48 hours of stroke onset and within 24 hours of initial magnetic resonance imaging (MRI) scan; both MRI and testing were obtained after any endovascular intervention or thrombolysis. Too few patients had both MRI and audiotaped picture description before intervention to evaluate associations before intervention. Additional inclusion criteria are as follows: (1) premorbid proficiency in English; (2) provided informed consent or indicated a decision maker to provide informed consent; and (3) ability to complete testing within 48 hours of onset. Exclusion criteria are as follows: (1) reduced level of consciousness or ongoing sedation; (2) neurological disease affecting the brain other than stroke; (3) inability to have MRI (eg, implanted ferrous metal); and (4) uncorrected visual or hearing loss. Most participants had exclusion criteria for thrombolysis or endovascular treatment; 7 of 67 patients had testing after they received intravenous tissue-type plasminogen activator; 1 patient had testing after endovascular treatment. The study protocol was approved by the Johns Hopkins Medicine Institutional Review Board.

MRI included diffusion-weighted imaging (DWI) and apparent diffusion coefficient to create the stroke map for analysis; fluid-attenuated inversion recovery and T2-weighted imaging to exclude other lesions; and susceptibility-weighted imaging to exclude hemorrhage. Sequences were acquired with whole-brain coverage using single-shot spin-echo echo planar imaging, in the transverse plane parallel to the AC-PC line. DWI was obtained as an average of diffusion-weighted echo planar images acquired in 3 orthogonal gradient directions with a b value of 1000 (s/mm^2); apparent diffusion coefficient was calculated from the diffusion-weighted echo planar images with a least diffusion weighting (b0).

Image Processing

We defined the boundary(s) of the acute stroke lesion(s) (hereafter, stroke map) using a threshold of >30% intensity increase from the unaffected area on DWI. The threshold was defined based on a previous study,[16] indicating that the acute lesion defined by a threshold of either 20% or 30% applied on DWI scanned on a 1.5-T scanner correlated well ($r \geq 0.8$) with the final infarct size after 1 week. We adopted the 30% threshold because the area defined by 20% threshold included more false-positive areas than that defined by the 30% threshold, in DWI scanned on a 3-T scanner like the one we used.[17] A neurologist (K.O.), masked to the behavioral data, manually modified the boundary to avoid false-positive and false-negative areas on RoiEditor (http://www.MRIstudio.org).[18] We then transformed the least DWI (b0) with T_2-weighted contrast to the JHU-MNI-b0 atlas using affine transformation followed by large deformation diffeomorphic metric mapping.[19,20] The resultant matrices were applied to the stroke map for normalization and overlaid on the customized version of the JHU-MNI Brain Parcellation Map (cmrm.med.jhmi.edu) to determine percent damage to each region of interest (ROI) using DiffeoMap (http://www.MRIstudio.org). We examined the following ROIs in each hemisphere: inferior frontal gyrus (pars opercularis, pars orbitalis, pars triangularis; IFGop, IFGorb, IFGtri), superior temporal gyrus (STG), middle temporal gyrus (MTG), inferior temporal gyrus (ITG), supramarginal gyrus (SMG), angular gyrus (AG), uncinate fasciculus (uncinate), sagittal stratum (SS), inferior frontal occipital fasciculus, and superior frontal occipital fasciculus. ROIs were selected on the basis of previous studies, indicating that they have a role in language processing[21–24] or higher level RH cognitive/communication functions.[25–29] Intraobserver and interobserver reliability of the stroke map, evaluated with 10 randomly selected images, were both excellent. The intraoperator Dice coefficient, used to evaluate the overlap of the stroke map was 0.90 (±0.044) with maps drawn with >6 months interval; the interoperator Dice coefficient calculated by 2 different observers (neurologist [K.O.] and radiologist [A.V.F.]) was 0.86 (±0.085). The intraclass correlation coefficient, used to evaluate the consistency of the stroke volumes, was 0.98 both within and across observers.

Analysis of Picture Description

Verbal descriptions of the Cookie Theft picture were recorded via microphone for subsequent transcription and analysis. Participants were asked to wear their eyeglasses. They were shown the picture and were instructed, "Please describe everything you see happening in this picture." There were no time limits. Recordings were stopped when the participants indicated they were finished. There is a published list of content units (CUs) often produced by healthy controls in describing this picture.[13,30] Individuals with aphasia produce fewer CU, fewer CU/minute, or more syllables/CU (because of intrusions, perseverations, and circumlocutions) than controls. Individuals with RH stroke often produce fewer CU, irrelevant CU, or more syllables/CU compared with controls because of irrelevant content, digressions, and perseverations (example is given in Table 1). They also produce a lower ratio of interpretive to literal CU[14]; interpretive CUs require some degree of inference (eg, mother versus woman or a statement about a disaster). Finally, patients with RH stroke produce a lower ratio of left:right CU (defined by the side of the picture on which the CU is depicted).[31] This ratio provides a sensitive measure

Table 1. Examples of Cookie Theft Picture Descriptions by Patients With Right Hemisphere and Left Hemisphere

Left hemisphere stroke: anomic, paraphasic
Their *mother**,† is getting to the *daughter**,† *giving**,† the *brother**,† a chance to sing. I'm…I'm… I'm a day. I can see it here. Time. The mother is going to the…the very dark and she is…at that *drying*†… dialup bead is in the son is that *reaching up*† and the daughter is er…die..er…[dalaralz]. Well that is the most.
Right hemisphere stroke: digressive, perseverative, inattentive, concrete, left neglect
A *window*.† *Curtains*.† Sorry. I'm okay I just can't cough. A window with a curtain. The stove, cabinet. A *yard*,† a garden, with some plantings. A curtain again. This, I'm going to assume, is a hot ring. I don't see a stove. I see more cabinets; here's another cabinet. And another window view of the garden. Another curtain. Maybe a hot plate or a stove.

*Interpretive content units.
†Content units.

of contralesional hemispatial neglect in both LH and RH stroke.[31] Excellent intrarater and inter-rater reliability in scoring CU, syllables, minutes, and percent interpretive CU has been reported.[14,30]

The NIHSS was administered by physicians certified in its administration on the same day as the picture description in all but 10 cases. In the remaining 10 cases, NIHSS score on the same day of the picture description was calculated from the documented neurological examination of the treating neurologist in the medical records using a validated method.[32] The score was calculated by a neurologist, certified in NIHSS administration, and masked to other behavioral and imaging data.

Statistics

One-way ANOVA was used to evaluate differences across groups (RH stroke, LH stroke, healthy controls, and differences in patients grouped by vascular territory) in age, total CU, syllables/CU, CU/minute, percent interpretive CU, and left:right CU. Then, differences between each pair of groups were tested with *t* tests. Differences between RH and LH stroke groups in lesion volume and NIHSS score were also tested with *t* tests. Pearson correlations were calculated between lesion volume and NIHSS, total CU, syllables/CU, CU/minute, and left:right CU to determine which variables were most strongly related to lesion volume in patients with RH and LH stroke, separately.

We tested the hypothesis that picture description analysis contributes valuable information about lesion volume, independently of the NIHSS, age, and sex. Separate multivariable regression analyses were run for patients with LH and RH stroke, with volume of infarct as the dependent variable, and the following independent variables: NIHSS, age, sex, total CU, syllables/CU, CU/minute, percent interpretive CU, and left:right CU. For most analyses, patients were separated by hemisphere of stroke because LH stroke and RH stroke have opposite effects on left:right CU and because we wanted to determine if these variables were equally effective in estimating infarct volume for LH and RH stroke. However, we also combined patients, omitting left:right CU as an independent variable. For patients with 0 right CU, a value of 0.5 CU was entered for right CU in calculating left/right CU because an infinite number could not be entered. For patients with 0 CU, a value of 0.5 was entered in calculating syllable/CU for the same reason.

To test the hypothesis that the Cookie Theft description contributes valuable information about lesion site independently of the NIHSS, linear regression analyses were run to determine which lesion sites were associated with each of the picture description variables and NIHSS, independently of lesion volume, age, and sex. Dependent variables were NIHSS, total CU, syllable/CU, CU/minute, left:right CU, and percent interpretive CU. These analyses were run separately for each hemisphere group because patients with LH stroke produce fewer CU and higher syllables/CU than controls for different reasons than do patients with RH stroke, so these variables are likely to be associated with different structures in the 2 hemispheres. Patients with LH stroke produce few CU or high syllables/CU when they are anomic; patients with RH stroke do so because of impaired selective and sustained attention. Independent variables for each of these multivariable regression analyses were lesion volume, age, sex, and percent damage to ≤5 of the following ROIs: inferior frontal gyrus (pars opercularis, pars orbitalis, pars triangularis; IFGop, IFGorb, IFGtri), STG, MTG, ITG, SMG, AG, uncinate fasciculus (uncinate), SS, inferior frontal occipital fasciculus, and superior frontal occipital fasciculus in the appropriate hemisphere for the patient group being evaluated. The ROIs selected for each variable (eg, NIHSS) were selected by determining in a univariate analysis those that were significantly correlated with the variable tested (eg, NIHSS) after Bonferroni correction for multiple comparisons.

To determine if the picture description could be practically used by clinicians, we provided <10 minutes of training in scoring picture descriptions to 1 stroke neurologist and 1 stroke fellow, not involved in the study. They were given 10 copies of the list of 56 CUs produced by normal speakers[13] and were asked to listen to randomly selected audiotapes of picture descriptions (5 from RH stroke; 5 from patients with LH stroke) and check off CU (the word/phrase or any word or phrase with the same meaning) produced by the speaker. Each CU is scored only once, even if the patient mentions it several times using the same or different words (eg, mother, mama, and mom). They were not permitted to replay the description (to simulate scoring the description live). There was 92.5% point-to-point percent agreement (agreed on minus disagreed on/total) in identifying the CU produced by the speaker. Scoring of each patient's description required these clinicians <2 minutes for each description. We determined how well total CU (this practical measure alone, which does not require taping or transcribing the description) accounted for lesion volume with and without NIHSS score with linear regression. We also evaluated the relationship between CU and NIHSS with vascular territory.

Vascular territory was identified by 2 neurologists (K.O. and A.E.H.). We grouped patients into the following vascular territory groups: internal carotid artery (middle cerebral artery+anterior cerebral artery or internal carotid artery watershed), anterior cerebral artery, middle cerebral artery (inferior division, superior division, or both, with or without lenticulostriate), posterior cerebral artery, and small vessel alone. There was 91.0% point-to-point percent agreement in identifying vascular territory; the 3 disagreements were resolved by a tie-breaker (third neurologist). We determined independent variables (CU, NIHSS score, age, and sex) that were significantly associated with odds of having a large-vessel anterior circulation stroke with logistic regression analysis. All statistics were run in Stata version 17.0.

Results

Demographics and mean scores for behavioral measures for each group are shown in Table 2. There were no significant differences between groups with respect to age (by ANOVA) or sex (by χ^2) or between stroke groups with respect to infarct volume or NIHSS (by *t* tests; Table 1). In contrast, 1-way ANOVA revealed significant differences between groups in the dependent variables of CU ($P<0.00001$), syllables/CU ($P=0.026$), CU/minute ($P<0.00001$), and left:right CU ($P=0.0001$).

Patients LH and RH with stroke produced fewer CU than the healthy controls ($t=-9.3$ for LH; $t=-5.6$ for RH; $P<0.00001$ for both), and patients with LH stroke produced slightly fewer CU than patients with RH stroke ($t=2.2$; $P=0.02$; Figure [A]). Moreover, patients with LH and RH stroke produced fewer CU/minute than the healthy controls ($P<0.00001$) but did not differ significantly from each other. Likewise, patients with LH and RH stroke produced more syllables/CU than healthy controls and did not differ significantly from each other (Figure [B]). The patients with LH stroke produced a higher ratio of left:right CU compared with patients with RH stroke ($P=0.0002$); and controls had a ratio that was midway between that of LH stroke and RH stroke, significantly different from both groups of patients with stroke (Figure [C]).

Predictors of Lesion Volume

Lesion volume negatively correlated with total CU in LH stroke ($r=-0.59$; $P=0.003$) and RH stroke ($r=-0.49$; $P=0.005$). Lesion volume also positively correlated with syllables/CU in LH stroke ($r=0.42$; $P=0.01$) and RH stroke ($r=0.60$; $P=0.0003$). Lesion volume negatively correlated with left:right CU only in RH stroke ($r=-0.48$; $P=0.005$). NIHSS also positively correlated with lesion volume in both LH stroke ($r=0.35$; $P=0.03$) and RH stroke ($r=0.67$; $P<0.0001$). For LH stroke, the strongest correlate of lesion volume was total CU; in RH stroke, it was NIHSS although syllables/CU was almost as high.

Table 2. Demographics and Mean (and SDs) for Behavioral Variables Across Groups

Dependent Variable	Left Hemisphere Stroke, Mean±SD	Right Hemisphere Stroke, Mean±SD	Healthy Controls, Mean±SD	Statistic	
					P Values
Sex	44% women	55% women	52% women	X^2=0.77	NS
Volume of infarct	20.7±33.9 cm^3	45.0±71.5 cm^3	n/a	*t*=1.8	NS
NIHSS score	4.2±0.5	5.4±0.9	n/a	*t*=1.19	NS
				ANOVA	
				F	*P* Value
Age, y	62.1±17.2	60.5±12.4	60.6±10.1	0.14	NS
Total CU	7.3±4.0	9.9±5.3	16.0±3.7	35.86	0.0000
Syllable/CU	11.9±13.3	8.5±6.6	6.2±1.9	3.80	0.0258
CU/min	17.4±14.1	18.3±12.5	44.5±21.1	29.64	0.0000
Left:right CU	1.53±1.1	0.78±0.63	1.19±0.43	10.24	0.0001
% interpretive CU	40.0±24.3	32.7±21.7	38.8±10.10	1.23	NS

CU indicates content unit; n/a, not applicable; NS, nonsignificant; and NIHSS, National Institutes of Health Stroke Scale.

Multivariable regression analyses revealed that in LH stroke, lesion volume was best accounted for by a model that included total CU, syllables/CU, left:right CU; CU/minute; NIHSS score, and age (r^2=0.59; *P*=0.002). Left:right CU and NIHSS each independently (*P*<0.01) accounted for some variance in lesion volume. In RH stroke, lesion volume was best accounted for by a model that included total CU, syllables/CU, left:right CU, percent interpretive CU, CU/minute, NIHSS score, and age (r^2=0.82; *P*<0.00001). Syllables/CU, NIHSS, and age each independently (*P*<0.001) accounted for some variance in lesion volume.

When we collapsed LH and RH stroke, lesion volume was accounted for by a model that included total CU, syllables/CU, percent interpretive CU, NIHSS score, and age (r^2=0.54; *P*<0.00001). Syllables/CU and NIHSS each independently (*P*<0.01) accounted for some variance in lesion volume. However, 48% of the variance in lesion volume could also be accounted for by total CU, NIHSS score, and age alone (r^2=0.48; *P*<0.00001). Total CU and NIHSS score each independently (*P*≤0.01) accounted for some variance in lesion volume.

Areas of Damage Associated With Each Behavioral Variable

In LH stroke, total CU was best accounted for by a model that included damage to left SMG, AG, ITG, MTG, STG, total infarct volume, and age (r^2=0.52; *P*=0.02). Percent damage to left inferior temporal gyrus (ITG) and infarct volume each independently (*P*<0.01) accounted for some variance in total CU. In LH stroke, NIHSS was best accounted for by a model that included damage to left caudate, putamen, AG, STG, MTG, ITG, SS, infarct volume, and age (r^2=0.66; *P*=0.003). Percent damage to left putamen and total infarct volume each independently (*P*<0.02) accounted for some variance in NIHSS.

In RH stroke, syllables/CU accounted for by percent damage to IFGop, MTG, ITG, age, infarct volume, and sex (r^2=0.82; *P*<<0.00001). Percent damage to right middle temporal gyrus (MTG), ITG, infarct volume, and age each independently (*P*<0.007) each accounted for some variance in syllables/CU. In RH stroke, percent interpretive CU accounted for by percent damage to right IFGop, SMG, AG, STG, SLF, SS, infarct volume (r^2=0.43; *P*=0.03). Percent damage to right AG and SS each independently (*P*=0.01) accounted for some variance

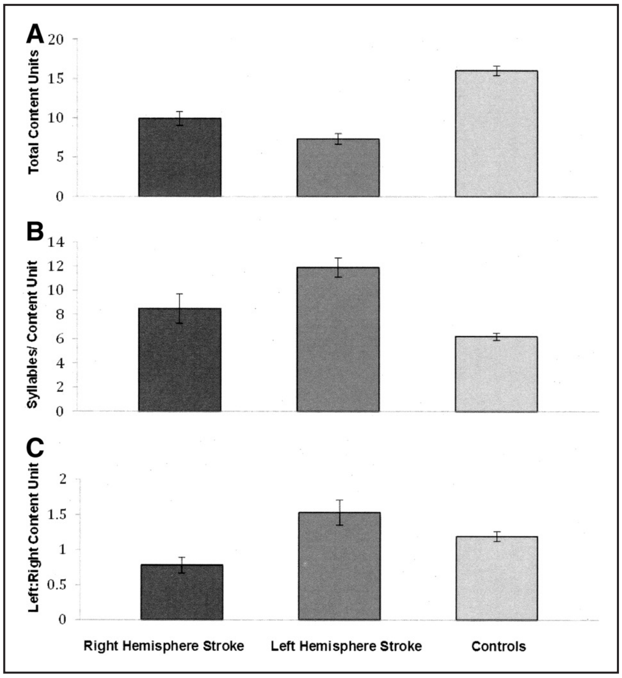

Figure. Mean performance by group on each picture description variable. Error bars show SE of the mean. **A**, Mean content unit (CU in each group. Right hemisphere (RH) stroke vs controls: *t*(degrees of freedom [df] 66)=−5.6; *P*<0.00001; left hemisphere (LH) stroke vs controls: *t*(df67)=−9.3; *P*<0.00001; RH vs LH stroke: *t*(df65)=1.79; nonsignificant. **B**, Mean syllables/CU in each group. RH stroke vs controls: *t*(df66)=2.0; *P*<0.05; LH stroke vs controls: *t*(df67)=2.5; *P*=0.01; RH vs LH stroke: *t*(df65)=−1.3; nonsignificant. **C**, Mean left:right CU in each group. RH stroke vs controls: *t*(df66)=−3.1; *P*=0.003; LH stroke vs controls: *t*(df67)=2.2; *P*=0.03; RH vs LH stroke: *t*(df65)=−3.9; *P*=0.0002.

in percent interpretive CU. In RH stroke, total CU accounted for by percent damage to right IFGop, SMG, AG, STG, SLF, SS, and infarct volume (r^2=0.48; *P*=0.01), but these were not independent of one another in relationship with total CU. In RH stroke, NIHSS accounted for by percent damage to putamen, caudate, anterior insula, STG, SLF, SS, age, volume, and sex (r^2=0.81; *P*<0.00001). Percent damage to caudate and putamen each independently (*P*<0.0001) accounted for some variance in total CU.

Vascular Territory

Characteristics of patient groups based on vascular territory are shown in Table 3. Patients with anterior cerebral artery and middle cerebral artery stroke were similar in CU and NIHSS score. When these 2 groups were collapsed into internal carotid artery branch occlusion, there was a significant difference (by ANOVA) in CU across vascular territories (*P*=0.048). Patients with any large-vessel anterior circulation stroke (internal carotid artery, middle cerebral artery, and anterior cerebral artery) also produced fewer CU than all other patients (mean, 10.2±4.4 versus 7.5±4.8; *t*(65)=2.2; *P*=0.03). In univariate logistic regression analyses, each increase in CU, evaluated as a continuous score, was associated with a reduced risk (odds ratio [OR], 0.88; 95% confidence interval [CI], 0.79–0.99; *P*=0.028) of large-vessel anterior circulation stroke, whereas each increase in NIHSS score was associated with an increased risk (OR, 1.37; 95% CI, 1.09–1.72; *P*=0.0004). In a multivariate model, CU was not associated with large-vessel anterior circulation stroke independently of NIHSS score. However, when syllable/CU and CU scores were evaluated in quartiles, each higher quartile of syllables/CU (OR, 1.91; 95% CI, 1.11–3.28; *P*=0.019) and each increase in NIHSS score (OR, 1.35; 95% CI, 1.08–1.68) were associated with increased risk of large-vessel anterior circulation stroke, independently of each other and independently of age and sex.

Discussion

Description of the Cookie Theft picture requires <2 minutes to score for CU and left:right CU (given a check list and minimal training) and only a few additional minutes to record, transcribe, and analyze for additional measures, such as syllables/CU. The simplest measure of total CU contributes independent information to the NIHSS score in estimating lesion volume. The full analysis of the picture description provides a rich source of information not currently captured by the NIHSS score and does not add to the administration time. Most importantly, analysis of the picture description measures some higher level RH cortical functions, beyond neglect, including attention, integration, and topic maintenance. The left:right CU measure efficiently quantifies hemispatial neglect after LH and RH stroke. Previous studies have shown that contralesional neglect may be as common in acute LH stroke as acute RH stroke,[33] and our study confirms a significant left:right bias in patients with acute LH stroke relative to controls. Right neglect in LH stroke may be less expected and less frequently noted and scored than left neglect in RH stroke on the NIHSS, so it is important to quantify.

Table 3. Relationship Between Vascular Territory and Clinical Variables

Vascular Territory	Total CU	Syllable/CU	CU/min	NIHSS Score
Internal carotid (n=5)	4.8±4.2	12.4±16.0	7.5±5.3	10.8±1.8
Anterior cerebral (n=3)	8.3±2.1	8.5±3.4	15.0±8.1	6.7±9.1
Middle cerebral (n=36)	7.8±5.0	11.6±10.6	14.7±10.4	4.9±4.0
Posterior cerebral (n=7)	8.4±5.5	9.1±4.7	19.4±14.2	3.1±1.6
Small vessel only (n=16)	4.8±4.2	6.0±3.7	29.1±15.4	2.1±1.4

CU indicates content unit; and NIHSS, National Institutes of Health Stroke Scale.

Other studies have identified regions of infarct associated with higher NIHSS scores although they have shown a stronger association between LH regions than RH regions.[8,34] One study compared several methods of lesion–symptom mapping, including multi-perturbation shapley value analysis,[35] voxel-symptom lesion mapping,[36] and volume of interest lesion–symptom correlation, and multi-area pattern prediction[37] for identifying regions associated with NIHSS score.[34] All of these approaches found the strongest association with left caudate and also left insula (2 areas where we also identified percent damage to be strongly associated with the NIHSS score in LH stroke). Two approaches identified an association between NIHSS and left frontal cortex or right frontal cortex. A recent study that controlled for lesion volume, age, and sex found that worse NIHSS scores in patients with LH stroke were associated with infarct in caudate, pallidum, putamen, insula, inferior frontal gyrus, precentral gyrus, postcentral gyrus, operculum, amygdala, and injury to white-matter tracts (corona radiata, internal and external capsules, superior longitudinal fasciculus, and uncinate fasciculus).[8] Worse NIHSS scores in RH stroke were not significantly associated with damage to particular sites, after controlling for age, sex, and lesion volume in that study. These studies are consistent with previous studies that have indicated that the NIHSS is more sensitive to LH function than RH function and is heavily weighted toward motor functions (more than cortical functions).[5,7,38] The current study also showed that NIHSS correlated with damage to predominantly motor regions (caudate and putamen) and white-matter tracts, whereas picture description variables correlated with damage to left and right regions in posterior frontal, temporal, and inferior parietal cortex. Therefore, the picture description analysis is complementary to the standard scoring of the NIHSS.

Finally, this expansion of the NIHSS may be especially valuable in settings where imaging is not available or not possible, to better estimate lesion volume.

One limitation of this study is that picture descriptions were not obtained in the hyperacute stage of stroke when it would be most useful to evaluate stroke severity. Except in cases eligible for thrombolysis or endovascular therapy, we evaluated the patients as soon as possible after admission for acute ischemic stroke (always within 48 hours of onset). We also did not evaluate change in NIHSS score and change in picture description variables to determine if these measures can effectively evaluate response to acute intervention. We will address these limitations in future studies. Another limitation is that we have not yet identified how these variables might be added to the current NIHSS score to measure stroke severity (as indicated by volume of infarct) most effectively.

Summary and Conclusions

The brief analysis of picture description we propose, which does not add administration time to the NIHSS, provides substantial additional information about both volume and location of ischemic stroke.

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