Clinical/Scientific Notes

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CHARACTERIZING RADIOLOGY REPORTS IN PATIENTS WITH FRONTOTEMPORAL DEMENTIA

Frontotemporal lobar degeneration (FTLD) is a common early onset dementing condition.[1] The subtypes of FTLD, behavioral variant frontotemporal dementia (bvFTD), and semantic dementia (SemD) have distinctive imaging patterns that separate them from healthy aging, Alzheimer disease (AD), and from each other.[2-4] The bvFTD causes frontotemporal tissue loss while SemD displays selective atrophy of the anterior temporal lobes.

We performed a retrospective analysis of MRI atrophy patterns in 40 patients with bvFTD.[5]

Methods. ***Participants.*** All patients evaluated between 1999 and 2006 at the UCSF Memory and Aging Center who consented to research, met the Neary research criteria for FTD,[5] and had an MRI scan within 1 year of presentation were included (figure e-1 on the *Neurology*® Web site at www.neurology.org). The referring diagnosis in patients' records and the radiologist's findings and impression on the first scan were recorded. Thirty-four scans were performed in academic settings and 6 in private centers.

Standard protocol approvals, registrations, and patient consents. We received ethics approval from the UCSF Research ethical standards committee on human experimentation and informed consent was obtained from all participants.

Test methods. Nine categories were identified based on the radiologist's reports of the 40 patients: 1) bvFTD, 2) white matter/ischemic disease, 3) AD, 4) normal pressure hydrocephalus (NPH)/hydrocephalus, 5) mitochondrial/metabolic, 6) encephalomalacia, 7) AD vs Pick, 8) atrophy, 9) unremarkable.

Twenty MRI scans from the patients with bvFTD were randomly selected and mixed with scans from 20 randomly selected patients with SemD,[5] 20 patients with probable AD (National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer's Disease and Related Disorders Association criteria),[6] and 20 research controls to verify that atrophy patterns can distinguish bvFTD from others. Two neuroradiologists blinded to patient's history, clinical diagnosis, radiologist's initial impression, and number of patients in each category rated the MRI scans as either bvFTD or non-bvFTD. The neuroradiologist's diagnosis was compared to the clinical diagnosis by calculating κ measures of agreement.[7]

Twenty scans were randomly selected for the interrater analysis: 9 atrophy, 1 bvFTD, 4 unremarkable, 1 mitochondrial/metabolic, 4 white matter/ischemia, and 1 hydrocephalus.

Statistical methods. Kappa statistics were calculated to measure rater agreement. The raters' diagnostic accuracy was determined by calculating sensitivity and specificity.

Results. ***Participants.*** The mean interval between symptom onset and first scan was 4.2 years (σ = 4.5 years; 0–24 years). Mean age at the time of the study was 64.2 years (σ = 10.2 years; 30–83 years). The most common symptom at onset was behavioral or personality changes or both (82.5%).

Test results. Pick disease or bvFTD was mentioned in 4 of 40 reports (10%) of patients with bvFTD (table). The characteristic atrophy pattern in bvFTD of frontotemporal and insular atrophy was described in 20 scans (50%); however, these scans were reported as "consistent with atrophy" with no mention of FTD or Pick disease. Other diagnoses ascribed to the MRI are shown in the table.

Only 11 of 40 patients with bvFTD had a clinical history on the MRI request and the 4 correctly identified MRI scans were in this category.

Estimates of agreement. Two blinded neuroradiologists categorized the MRI scans of patients clinically diagnosed with bvFTD, AD, and SemD and normal control subjects into bvFTD vs non-bvFTD with a 97% specificity (95% confidence interval [CI] = 0.88–0.99) and 61% sensitivity (95% CI = 0.36–0.82) by the first rater and 100% specificity (95% CI = 0.93–1.00) and 60% sensitivity (95% CI = 0.36–0. 80) by the second. There was substantial agreement between the raters and the categorical clinical diagnoses of bvFTD and non-bvFTD (κ = 0.67; 95% CI = 0.48–0.87) for the first rater and (κ = 0.69; 95% CI = 0.50–0.89) for the second. There was good agree-

Supplemental data at www.neurology.org

Table Radiologist diagnostic impressions in 40 patients clinically diagnosed with behavioral variant frontotemporal dementia (bvFTD)

Reported diagnosis	No. (%)
Atrophy	20 (50)
Unremarkable	5 (12.5)
White matter/ischemic	6 (15)
bvFTD	3 (7.5)
Alzheimer disease vs Pick disease	1 (2.5)
Alzheimer disease	1 (2.5)
Normal pressure hydrocephalus/ hydrocephalus	2 (5)
Encephalomalacia	1 (2.5)
Mitochondrial/metabolic	1 (2.5)

ment between raters (κ = 0.78; 95% CI = 0.59–0.96).

Discussion. Radiologists infrequently propose bvFTD or Pick disease as the diagnosis on MRI and in only 10% of cases was the correct diagnosis even considered. The MRI changes were not subtle as 2 neuroradiologists identified the atrophy pattern of bvFTD with nearly 100% specificity and sensitivity in the 60% range.

Incorrect diagnoses can impact care. Calling an atrophy pattern unremarkable may lead to disregard of symptoms or diagnosis of psychiatric disorder, thus delaying appropriate treatments. Misdiagnosis of hydrocephalus, vascular disease, or another dementia can lead to potentially harmful interventions. Although focal atrophy may not be evident early in the disease, most patients with bvFTD present later because subtle behavioral changes are often overlooked or ascribed to mood disorder. A negative scan, however, does not exclude the diagnosis of bvFTD.

Diagnostic accuracy improved when clinicians included a patient's clinical history, suggesting that better communication between clinicians and radiologists should improve diagnosis.

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Supported in part by NIH grant 1TL1RR024129-03 and the Doris Duke Charitable Foundation.

Disclosure: J. Suarez received a fellowship stipend from UCSF, PACCTR program. Dr. Tartaglia, Dr. Vitali, Dr. Erbetta, Dr. Neuhaus, V. Laluz, and Dr. Miller report no disclosures.

Received February 20, 2009. Accepted in final form June 2, 2009.

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Statistical analysis was conducted by Dr. John Neuhaus.

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MOST STROKE PATIENTS DO NOT GET A WARNING: A POPULATION-BASED COHORT STUDY

In longitudinal studies with active outcome surveillance, the 3-month risk of stroke after TIA is approximately 17%.[1] Recent reports suggest that expedient management of TIA can reduce this risk by as much as 80%.[2,3] For such a strategy to have a major impact on the burden of cerebrovascular disease in the general population, stroke with preceding TIA must be a relatively common occurrence. Using data from the Registry of the Canadian Stroke Network (RCSN), we sought to ascertain the frequency, characteristics, and outcomes of acute stroke patients with a prior TIA.

Methods. We prospectively identified consecutive patients with a final diagnosis of acute stroke admitted to 12 Ontario hospitals through data recorded in the RCSN (accrual interval July 1, 2003, to September 30, 2007). Chart validation studies have shown excellent agreement with the RCSN database, with duplicate data abstraction performed on a random sample of 10% of charts. Patients with in-hospital strokes (n = 78) or unknown final diagnosis (n =

Table Characteristics of acute stroke patients with or without previous TIA

Characteristic	Patients with previous TIA (n = 2,032)	Patients without previous TIA (n = 14,377)
Demographic factors		
Age, y	77 (68–83)	72 (59–81)
Sex (female)	962 (47.3)	7,103 (49.4)
Living alone prestroke	395 (19.4)	2,664 (18.5)
Independent prestroke	1,535 (75.5)	10,155 (70.6)
Widowed	532 (26.2)	2,875 (20.0)
Language (English)	1,742 (85.7)	12,178 (84.7)
Stroke typology		
Hemorrhagic	192 (9.4)	4,027 (28.0)
Ischemic	1,840 (90.6)	10,350 (72.0)
Large artery	367 (18.1)	1,423 (9.9)
Cardioembolic	382 (18.8)	2,310 (16.1)
Lacunar	299 (14.7)	1,845 (12.8)
Other	60 (3.0)	539 (3.7)
Undetermined	732 (3.6)	4,233 (2.9)
Medical history		
Diabetes mellitus	558 (27.5)	2,967 (20.6)
Previous stroke	637 (31.3)	2,360 (16.4)
Hypertension	1,537 (75.6)	8,262 (57.5)
Hyperlipidemia	878 (43.2)	3,873 (26.9)
Current smoker	306 (15.1)	2,666 (18.5)
Family history of stroke	183 (9.0)	1,006 (7.0)
Intracranial bleed	47 (2.3)	259 (1.8)
Carotid intervention	95 (4.7)	139 (1.0)
Heart failure	199 (9.8)	1,003 (7.0)
Angina	547 (26.9)	2,475 (17.2)
Peripheral arterial disease	175 (8.6)	672 (4.7)
Atrial fibrillation or flutter	491 (24.2)	2,826 (19.7)
Myocardial infarction	348 (17.1)	1,607 (11.2)
Coronary intervention	222 (10.9)	1,039 (7.2)
Venous thromboembolism	64 (3.1)	312 (2.2)
Valvular heart disease	110 (5.4)	504 (3.5)
Valve replacement	46 (2.3)	232 (1.6)
Dementia	244 (12.0)	1,054 (7.3)
Asthma or emphysema	308 (15.2)	1,417 (9.9)
Cancer	206 (10.1)	1,132 (7.9)
Arthritis	535 (26.3)	2,476 (17.2)
Depression	105 (5.2)	648 (4.5)
Peptic ulcer disease	149 (7.3)	615 (4.3)
Existing hemiplegia or paraplegia	1,086 (53.4)	7,116 (49.5)
Charlson comorbidity index >1	881 (43.4)	3,967 (27.6)
Final disposition		
In-hospital death	258 (12.7)	2,182 (15.2)
Rankin score ≥3	1,186 (58.4)	8,632 (60.0)
Discharged home	875 (43.1)	5,769 (40.1)

Continuous variables are reported as median (interquartile range) and categorical variables as n (%).

615) were excluded. Further details regarding the RCSN have been published elsewhere.[4,5]

Standard protocol approvals, registrations, and patient consents. The study was approved by the Sunnybrook Health Sciences Research Ethics Board and the Privacy Office of the Canadian Stroke Network; the requirement for written informed consent from participants was waived under Ontario privacy legislation.

Results. Of 16,409 consecutive patients with a final diagnosis of acute stroke in the RCSN, 2,032 (12.4%) had a prior TIA (ischemic neurologic deficit lasting less than 24 hours). Those with large artery ischemic stroke were most likely to have a previous TIA (20.5%), whereas patients with hemorrhagic stroke (4.6%) were least likely; 15.1% of ischemic stroke patients had a previous TIA. Patients with previous TIA were typically older than patients without previous TIA and more likely to have diabetes, hypertension, atrial fibrillation, angina, peripheral arterial disease, and heart failure (table). Conversely, patients without prior TIA were significantly more likely to die during their hospital stay (15.2% vs 12.7%; $p = 0.003$), experience an in-hospital cardiorespiratory arrest (4.8% vs 3.1%; $p < 0.001$) or seizure (2.7% vs 1.5%; $p = 0.002$), and were less likely to be discharged to home (40.1% vs 43.1%; $p = 0.012$). After multivariable adjustment, lack of prior TIA continued to predict poor prognosis (for example, a 14% reduction in the odds of being discharged home, 95% confidence interval 5 to 22). These findings may be due to a lack of ischemic preconditioning in patients without prodromal TIA.[6]

Discussion. A key limitation of our work is that we did not have information on the timing of prodromal TIA; however, previous data suggest that such events are most likely to occur within the week immediately preceding the stroke.[7] In summary, only 1 in 8 patients with acute stroke had a previous TIA (with a higher frequency of TIA in large artery stroke). Widely implemented urgent TIA clinics might therefore prevent a small but significant fraction of the current stroke burden. In addition, these data highlight a need for risk profiles that accurately identify and stratify individual risk for first stroke.

AUTHOR CONTRIBUTIONS

Statistical analysis was conducted by Julie T. Wang, Institute for Clinical Evaluative Sciences, Toronto, Canada.

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eral Internal Medicine and Women's Health Program (M.K.K.), University Health Network, Canada.

The study was sponsored by the Canadian Institutes of Health Research and Ontario Ministry of Health and Long-Term Care. The Registry of the Canadian Stroke Network was sponsored by the Canadian Stroke Network and the Ontario Ministry of Health and Long-Term Care. The funding sources had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; or preparation, review, or approval of the manuscript.

Disclosure: Dr. Hackam, Dr. Kapral, Ms. Wang, and Dr. Fang report no disclosures. Dr. Hachinski serves as Editor-in-Chief of Stroke and has received honoraria for participation in symposia from Ferrer Group and Boehringer-Ingelheim.

Received March 9, 2009. Accepted in final form May 19, 2009.

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