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Meet the Resident & Fellow Editors of Neurology
And learn how you can contribute to the journal at the Residents & Fellows Career Forum and Reception
Monday, March 18, 2013, 7:30–9:00 p.m.
San Diego Marriott Marquis & Marina, Marriott Hall
Announcement

*Neurology*® Resident and Fellow Section Writing Award

The winners of the 2013 Awards are:
Daniel R. Gold, DO, and Stephen G. Reich, MD
Clinical Reasoning: A 55-year-old woman with vertigo: A dizzying conundrum
*Neurology* October 23, 2012 79:e146-e152
See page 10

The winners will be honored at the 2013 AAN awards luncheon. See page 10 of this Highlights booklet for the award-winning article.

The *Neurology* Resident and Fellow Section Writing Award is intended to recognize the extraordinary writing abilities of those currently in training in neurology. Eligible manuscripts will include any submitted to and published in the *Neurology* Resident and Fellow Section, whether online or in print. Submissions on any topic of interest to trainees and in any subcategory of the section will be eligible. The main criteria for selection will be educational value, novelty, depth of exposition, and clarity of writing. At least one author of the manuscript must be currently in a neurology residency program or in fellowship training in one of the neurological subspecialties. All authors will be considered equal recipients of the award in order to recognize and encourage collaborative work among trainees. The next award will be announced in early 2014 and will be awarded for a paper published in 2013.

No formal application process is required. All manuscripts submitted to the section will be considered. Manuscripts should be submitted online at www.neurology.org. Please direct any questions to kpieper@neurology.org.

PAST RECIPIENTS

**2012 Award Winner**
Christina B. Pham, Johannes R. Kratz, Angie C. Jelin, and Amy Gelfand
*Neurology* August 16, 2011 77:695-697

**2011 Award Winner**
Amy Gelfand, MD, for Right Brain: We were all once ‘fixed and dilated’.
*Neurology* November 16, 2010 75:1851-1852

**2010 Award Winner**
H. Aitken, G. Gorman, MRCP, R.; McFarland, MRCPCH; M. Roberts, FRCP; R.W. Taylor, FRCP, and D.M. Turnbull, FRCP for Clinical Reasoning: Blurred vision and dancing feet
Restless legs syndrome presenting in mitochondrial disease.
*Neurology* May 5, 2009 72:e88-e90

**2009 Award Winner**
Megan Alcauskas, MD, and Rita Charon, MD, PhD, for Right Brain: Reading, writing, and reflecting: Making a case for narrative medicine in neurology.
*Neurology* March 11, 2008 70:891-894
The **Neurology** Resident and Fellow Section

Mitchell S.V. Elkind, MD, MS, FAAN; John J. Millichap, MD

The *Neurology*® Resident and Fellow Page was launched in 2004 with the goal of providing a forum for trainees and educators to write about topics relevant to residency and fellowship, including academic research projects, practice, ethics, teaching, historical topics, and international training experiences. The “page” has since evolved into a major section of the journal, with articles appearing weekly. Though most are published online, exceptional articles also appear in the print journal. The number of submissions to the section has increased dramatically (from 12 in 2004 to 429 in 2012), and the quality of published manuscripts has improved (represented by our current acceptance rate of about 25%). We published 138 manuscripts in 2012, our highest number to date.

**Neurology Resident and Fellow Section Submissions and Acceptances 2004–2012**

The Resident and Fellow Section (R&FS) is trainee-run: a nationally representative team of 15 residents and fellows, each of whom serves three years, has responsibility for reviewing, editing, and publishing articles of interest to trainees. Residents will be selected annually, with requests for applications occurring in the late summer. This provides an opportunity for these trainees to begin a process of lifelong learning about writing, reviewing, and identifying articles of importance to the field. Section members also write articles, but the vast majority of manuscripts are written by neurology trainees, program directors, and educators around the world. Photographs and brief biographies of the current Resident and Fellow Section Editorial Team may be found in this Highlights booklet.

The Section has several different subsections, and many are represented by the articles in this booklet. These include Emerging Subspecialties in Neurology, Clinical Reasoning, Right Brain, Child Neurology, Journal Club, Pearls and Oysters, International Issues, Education Research and Initiatives, Teaching Neuroimages (including both static images and videos), and Book and Media Reviews. The descriptions of the subsections appear before each sample article.

The group has also initiated and developed numerous other unique projects since the inception of the Section, including a website, podcasts, weekly electronic communications, an annual writing award, Mystery Cases, Call for Authors, and other new subsection ideas. Podcasts related to articles published in the RFS began in December 2007, for example, and weekly E-Pearls, now archived on our website, have been sent to residents nationwide since July 2008. The first annual RFS writing award was awarded in April 2009, the first Mystery Case published in August 2009, our website launched in 2010, and the first journal club articles published in August 2011. In 2011, we expanded our book review section to a new Media and Books Reviews Section to provide reviews of other forms of educational media in increasing use, including websites and apps. Our new Call for Authors program, in which trainees throughout the world have the opportunity to sign up to write articles on selected topics, was launched in January 2012. In 2012 we also began making available all Teaching Neuroimages as teaching slides.

The Section has been strongly supported by *Neurology*’s Editors-in-Chief, Associate Editors, editorial staff, the American Academy of Neurology, and the publishers Lippincott Williams and Wilkins. In particular, Kathy Pieper, Sandi Moriarity, and Robert Witherow have provided continual assistance and encouragement without which the Section could not have survived.
The *Neurology* Resident and Fellow Section

*Continued from page 1*

*Neurology* recognizes that the future of the journal, and the future of the field of neurology itself, depends on the interest and commitment of its readers and writers. This journal is one of the most important records of our profession, and current trainees are the profession’s most valuable resource. We anticipate further developments for the R&FS in the future, limited only by the imagination of the students, residents, fellows, and others who are interested in neurology education.

We welcome submission of manuscripts for the Resident and Fellow Section, and author instructions can be found at [www.neurology.org](http://www.neurology.org). Papers submitted for this Section will undergo the same thorough peer review process as all *Neurology* submissions, and it is anticipated they will reflect the same high level of quality. It is further expected that manuscripts published in the Section will carry the same academic weight, whether on-line or in print, as papers published elsewhere in *Neurology*. We also continue to welcome input from our readers, including program directors and other educators, on features that will be most valuable. Questions and comments should be addressed to Mitchell Elkind, John Millichap, or Kathy Pieper at kpieper@neurology.org.

We hope you enjoy this year’s edition of the Highlights of the R&FS!

Mitchell S.V. Elkind, MD, MS, FAAN, FAHA, Associate Editor, Resident and Fellow Section

John J. Millichap, MD, Deputy Associate Editor, Resident and Fellow Section

This R&F Highlights Booklet is also available in PDF format on the iPad® and mobile versions of *Neurology*!
Top 10 Ways for Program Directors to Use the *Neurology* Resident & Fellow Section (R&FS)

Victoria S.S. Wong, MD, and John J. Millichap, MD

Visit the Resident & Fellow Section website at [http://neurology.org/site/feature/index.xhtml](http://neurology.org/site/feature/index.xhtml) to access the features below.

1. Starting this year, every Teaching NeuroImage published will have a supplemental PowerPoint slide set available for download from the *Neurology*® website that may be used for group presentations.

2. A one-hour resident conference can easily be filled by reviewing a Clinical Reasoning article. The piece is formatted for teaching and has sections with questions for consideration. E-Pearls are ideal for brief educational exercises.

3. Journal Club articles provide critical appraisals of articles published in *Neurology*. The format is ideal for guiding discussions at your institutional Journal Club meetings.

4. The Career Choices section is a good starting point for residents applying for fellowship positions. In addition to an article about the fellowship search, the Emerging Subspecialties in Neurology section discusses additional avenues for training, and the website provides a link to the AAN Fellowship Directory.

5. The Media and Book Reviews section may provide ideas for what to purchase with book funds. In addition to traditional texts, the R&FS will also review neurology apps and other electronic media.

6. To follow the R&FS on Facebook, join our group entitled 'American Academy of Neurology Residents and Fellows.' For further digital access to R&FS content, download the *Neurology* app onto your iPad®, listen to the weekly *Neurology* podcast which includes the E-Pearl of the week, and follow *Neurology* Twitter for updates.

7. The Right Brain subsection allows you to exercise your right brain by composing your neurological narratives and submitting them.

8. The Education Research section reports quality research on educational topics including surveys of program directors and residents, as well as studies about educational interventions and resident evaluation.

9. Scholarly activity among residents and fellows can be promoted by encouraging them to write for the R&FS. Refer to the ‘Call for Authors’ page on the website for ideas to jump-start the writing process. Keep in mind that all published articles are considered for the Annual Resident & Fellow Writing Award.

10. Pick up a few more copies of this R&FS Highlights book and help to spread the word! Encourage your trainees to read the R&FS regularly, send us manuscript submissions, and apply for a position on our editorial team during our annual recruitment!
Mitchell S.V. Elkind, MD, MS, FAAN

Dr. Elkind graduated from Harvard Medical School in 1992, interned at Brigham and Women’s Hospital, and completed neurology residency at Massachusetts General Hospital. He then obtained a Masters degree in Epidemiology from Columbia University while doing his clinical stroke fellowship. Currently, Dr. Elkind is an Associate Professor of Neurology and Epidemiology at Columbia University in the Division of Stroke and the Associate Chair for Clinical Research and Training. His research is focused on inflammatory and infectious biomarkers in stroke risk prediction, as well as acute stroke therapy. Dr. Elkind is a Principal Investigator of 3 NINDS independent investigator awards. These include NeuSTART (Neuroprotection with Statin Therapy for Acute Recovery Trial), a clinical trial evaluating short-term high-dose statin therapy in acute stroke; Levels of Inflammatory Markers in the Treatment of Stroke (ULIMITS), a multi-center blood biomarker study among lacunar stroke patients participating in the S3PS trial; and the Northern Manhattan Study, a prospective cohort study of stroke risk factors. He is the former Neurology Residency Program Director at Columbia University Medical Center, and is a fellow of the American Academy of Neurology and a member of the American Neurological Association and the Stroke Council of the American Heart Association. He has mentored several residents and fellows in neurology and clinical research.

Miya Bernson-Leung, MD

Miya Bernson-Leung received her undergraduate degree from Harvard College and her medical degree from Harvard Medical School. She is now training in child neurology at Boston Children’s Hospital following her pediatrics residency in the Boston Combined Residency in Pediatrics. Interests include medical education at the student and resident level, and the promotion of cross-disciplinary communication and creative writing in medicine. Future areas of exploration include neuromuscular disorders and pediatric stroke.

Audrey Brumback, MD, PhD

Audrey Brumback is a Child Neurology fellow at the University of California, San Francisco. She earned her MD and PhD degrees at the University of Colorado School of Medicine, where she studied the role of chloride transporters in neonatal seizures. Her current research interests include mechanisms of inhibition and the function of ion transporters in normal and diseased brains.

Joseph Cahill, MD

Joseph Cahill is a second year neurology resident at the University of Wisconsin. Originally from Oklahoma, he attended medical school at the Universidad Autonoma de Guadalajara in Guadalajara, Mexico after serving eight years as an active duty Hospital Corpsman in the US Navy. He can now say he is a bilingual, bicultural physician. He is also a screenwriter whose credits include, Manipulating Life, a short film produced in 2008 that was shown in festivals within the US. He has yet to write that Oscar winning feature film. He is currently serving as an active duty Navy Lieutenant and plans to retire at a young age somewhere off the coast of Mexico. His other interests include traveling and competitive beach volleyball.

Daniel Goldenholz, MD, PhD

Daniel Goldenholz completed his MD and PhD training at Boston University where his thesis work focused on multimodal imaging techniques for brain mapping and epilepsy. He then completed a one year post-doctoral fellowship at the Harvard/MIT/MGH Martinos Imaging Center, studying techniques in functional MRI, diffusion tensor imaging, transcranial magnetic stimulation, and near-infrared spectroscopy. He completed his internal medicine internship at Alameda County Medical Center and is currently a neurology resident at UC Davis Medical Center.

Jeremy Gregory, MD

Jeremy Gregory studied biochemistry, biophysics, and Spanish at Oregon State University and then medicine at Mayo Medical School. He is currently a resident in the adult neurology program at Mayo Clinic in Rochester, Minnesota. His academic interests include movement disorders, prion diseases, art in medicine, and teaching and education research.

Cliff Hampton, MD

Cliff Hampton is a PGY-2 Neurology resident at the University of Colorado in Denver. He graduated from Weber State University in Ogden, Utah with a degree in Spanish Language and obtained his medical degree from Baylor College of Medicine in Houston, Texas. In addition to general neurology, he is also interested in bioethics and its relationship to the field of neurology.
Andrea Harriott, MD, PhD

Andrea Harriott is a neurology resident at Mayo Clinic in Jacksonville, FL. She earned a Bachelor of Science degree from Morgan State University. She earned her MD and PhD degrees from University of Maryland in Baltimore, MD. Her thesis was completed in the Pittsburgh Center for Pain Research where she investigated ion channel mechanisms of dural afferent sensitization and migraine using patch clamp electrophysiology. Recent research endeavors include investigating associations between genetic variants, migraine and stroke risk. She continues her research with academic interests in headache, and stroke. She enjoys teaching, community outreach, and mentoring.

Shaheen E. Lakhan, MD, PhD, ME, MS

Shaheen Lakhan is a Clinical Instructor of Medicine [Neurology] at the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University. After graduating from medical school at the Technion - Israel Institute of Technology, he entered neurology residency training at the Cleveland Clinic. He is Executive Director of the Global Neuroscience Initiative Foundation, on the editorial board of several BioMed Central publications, and instructor of functional neuroanatomy at UCLA Extension. As a member of the American Academy of Neurology’s Distance Learning Subcommittee, he develops online educational courses for neurologists, neuroscientists, and trainees.

Matthew R. Lincoln, MD, DPhil

Matthew Lincoln is a PGY2 neurology resident at the University of Toronto. He is a graduate of Harvard College and earned his MD at the University of Toronto. He completed his DPhil at the University of Oxford, where he studied the genetics of multiple sclerosis. Current research interests include multiple sclerosis and the history of neurology.

Dragos Nita, MD, PhD

Dragos Nita graduated from ‘Carol Davila’ University in Bucharest, Romania. He earned his PhD from Laval University in Quebec, Canada, where he studied the cellular and network mechanisms of post-traumatic epileptogenesis and the relationship between seizures and different states of vigilance under the supervision of Prof. Mircea Steriade. Since 2008, he has been a pediatric neurology resident at the University of Toronto and The Hospital for Sick Children in Toronto, Canada. His academic interests include epilepsy, neurophysiology, and pediatric neuro-intensive care and sleep medicine.

Adam Numis, MD

Adam Numis is a child neurology fellow at the University of California, San Francisco. He is a graduate of Harvard Medical School and completed his pediatrics training at Boston Children’s Hospital/Boston Combined Residency Program. His academic interests include epidemiological and translational investigations in pediatric epilepsy and neurocritical care. He also has an interest in issues related to advocacy and education.

James H. Park, MD, PhD, MPhil

James H. Park is a resident at the Barrow Neurological Institute. He completed his MD PhD at Yale University with research focusing on Alzheimer’s disease. He received an MPhil in Biochemistry at Cambridge and an MPhil in Chemistry at Harvard. His academic interests include neurodegeneration and neuroregeneration.

Peter Pressman, MD

Peter Pressman graduated from Oregon Health & Science University, and completed neurology residency at Northwestern Memorial Hospital in Chicago. He is now in fellowship training at the Memory and Aging Center at the University of California, San Francisco, where he is pursuing his academic interests in functional connectivity, dementias, and medical education.

Andrew Schepmyer, MD

Andrew Schepmyer completed his Bachelor of Health Sciences degree at McMaster University in Hamilton, Ontario in 2007, and then went on to earn his medical degree at the University of Toronto in 2011. He is currently in the second year of his adult neurology residency at the University of British Columbia in Vancouver. His academic interests include autoimmune and infectious diseases of the nervous system as well as medical education.

Roy E. Strowd, III, MD

Roy Strowd graduated from Duke University in 2001 where he studied attentional processing in the visual system. He completed his Doctor of Medicine at the Wake Forest University School of Medicine and has continued at Wake Forest where he is currently a PGY-III neurology resident. Current research interests include the use of process-oriented and other alternative preparation strategies in medical education, motor and non-motor side effects of deep brain stimulation and vaccination efficacy in neuro-oncology patients.
Mystery Case

Interesting teaching cases submitted to the Resident & Fellow Section are chosen by the Resident & Fellow Editors to be published under the new Mystery Case subcategory. The Neurology Editorial Office disseminates a teaser through social media before the case is published. This usually includes a short description of the case, video or partial figure, and 1-3 questions. Responses are compiled and then published with the full case.
Teaching NeuroImages: 
A prematurely aging patient presenting with severe leukoaraiosis and stroke

Figure 1 Photograph of the patient with Werner syndrome

The patient appears older than her age (A). Her hands have tight, scleroderma-like skin (B).

A 27-year-old woman presented with sudden onset left-sided numbness and double vision. In the last 10 years, she developed diabetes mellitus, cataract, osteoarthritis, osteoporosis, benign neoplasm of the skull, epilepsy, and nonscarring alopecia. Her parents were first-degree relatives and there were no relatives with similar disease. On examination there were right internuclear ophthalmoplegia, short stature, tight skin, hyperkeratosis (figure 1), cataract, and mild cognitive impairment. Brain MRI disclosed acute brainstem ischemic infarct and severe leukoaraiosis with multiple old lacunar infarcts secondary to small-vessel disease (figure 2). Antinuclear antibodies and anticycadioplin and lupus anticoagulant antibodies were normal or negative. Genetic testing was not available.

The patient presents with 5 cardinal and 3 minor features of Werner syndrome, which is an unusual autosomal recessive inherited disorder caused by mutations in the WRN gene on chromosome 8.1 It encodes a protein with helicase and exonuclease activities, absence of which leads to abnormalities in several DNA repair and processing pathways. Werner syndrome is the most common adult-onset progeria. The disease is characterized by premature aging and propensity for cancer.1

Werner syndrome is an uncommon cause of stroke, but it should be considered in young patients with premature aging.2

AUTHOR CONTRIBUTIONS
Dr. Seixas, Dr. Baiense: design or conceptualization of the study. Dr. Seixas, Dr. Pedroso, Dr. Fukuda, Dr. De Figueiredo, Dr. Baiense, Dr. Yared, Dr. Ferraz, Dr. Barsottini: analysis or interpretation of the data. Dr. Seixas, Dr. Pedroso, Dr. Fukuda, Dr. De Figueiredo, Dr. Ferraz, Dr. Barsottini: drafting or revising the manuscript for intellectual content.

REFERENCES

MYSTERY CASE RESPONSES
The Mystery Case series was initiated by the Neurology® Resident & Fellow Section to develop the clinical

From the Department of Neurology and Neurosurgery, Universidade Federal de São Paulo, São Paulo, Brazil. The authors report no disclosures relevant to the manuscript. Go to Neurology.org for full disclosures.
Brain MRI diffusion-weighted imaging and apparent diffusion coefficient disclosed small area of restricted diffusion on right pons (A). Fluid-attenuated inversion recovery sequence showed diffuse subcortical hyperintensity (B) and susceptibility-weighted imaging showed numerous hypointense lesions suggesting microhemorrhages (C). These findings are suggestive of small-vessel disease.

reasoning skills of trainees. Residency programs, medical student preceptors, and individuals were invited to use this Mystery Case as an educational tool. Responses were solicited through a group e-mail sent to the American Academy of Neurology Consortium of Neurology Residents and Fellows and through social media (Facebook and Twitter).

The answers that we received for this Mystery Case came from 3 different continents through e-mail and social media, in English and Spanish, and from individual residents rather than groups. All of them were well-reasoned and thoughtful.

Many respondents (46%) correctly identified Werner syndrome or adult progeria based on the concomitant occurrence of multiple pathologies characteristic for premature aging in a rather young patient. The second most common diagnosis (20%) was cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencephalopathy. Other diagnostic considerations included Cockayne syndrome (cachectic dwarfism, photosensitivity, progeroid appearance, pigmented retinopathy, sensorineural hearing loss, and progressive neurologic degeneration), Rothmund-Thomson syndrome (photosensitivity, poikilodermatous skin changes, cataracts, skeletal dysplasias, and predisposition to osteosarcoma and skin cancer), as well as systemic lupus erythematosus, myotonic dystrophy, and proteus syndrome.

This Mystery Case illustrates a rare cause of stroke that should be considered in young patients with premature aging.

Dragos A. Nita, MD, PhD
The Hospital for Sick Children, Toronto, Canada
Clinical Reasoning focuses on case presentations with the aim of developing clinical reasoning skills among trainees. Appropriate cases for publication would include uncommon presentations of common neurological disorders and also typical presentations of more exotic disorders. The emphasis of the case presentation should be on generating a sound, thorough differential diagnosis; logically arriving at the correct diagnosis; and thoughtfully discussing the teaching-points of the case. Cases discussed in the section should utilize data presented serially in two to four segments that could be opened sequentially by the reader, allowing them to challenge themselves by thinking through the differential diagnosis or treatment options at each step. The manuscript should indicate where each break would occur, with specific questions for the reader to consider as they work their way through the case. The final section should provide the experienced clinician’s discussion (or resident author’s literature review). Ideally the individual sections will also include visually presented data, such as radiology, EEG, EMG, or other studies.
Clinical Reasoning:
A 55-year-old woman with vertigo
A dizzying conundrum

SECTION 1
A 55-year-old woman presented to the emergency department complaining of dizziness. Several hours earlier she abruptly felt "the room spinning and moving back and forth." Simultaneously, she experienced nausea, vomiting, and gait unsteadiness. The dizziness exacerbated with head movement. She denied head or neck pain, photophobia, phonophobia, auditory symptoms, weakness, numbness, diplopia, dysarthria, dysphonia, dysphagia, history of recent illness, prior dizziness, or headache. Medical history included hyperlipidemia and hypertension.

Question for consideration:
1. What is the differential diagnosis for acute vertigo?

SECTION 2
To determine the cause of acute vertigo, it is important to know whether it is transient (seconds to minutes) or prolonged (hours to days); a single episode of vertigo or a recurrence; if it is positionally provoked (e.g., benign paroxysmal positional vertigo); and if there are any accompanying symptoms or signs. The most common causes of acute prolonged vertigo include a peripheral vestibulopathy, Ménière syndrome, migrainous vertigo, or brainstem or cerebellar ischemia. This discussion is limited to the distinction between a peripheral vestibulopathy and ischemia.

The acute vestibular syndrome (AVS) develops over seconds to hours and is characterized by vertigo, nausea, vomiting, gait instability, head motion intolerance, and nystagmus. It is caused by either an acute peripheral vestibulopathy (APV) or brainstem/cerebellar ischemia, and similarities in presentation often make the distinction a diagnostic challenge. Transient ischemic attacks can cause acute vertigo with rapid resolution but vertigo resulting from a stroke, like an APV, may last days to weeks. Vertigo caused by ischemia is almost always accompanied by other neurologic symptoms and signs but may occur in isolation.

An APV is characterized by acute prolonged vertigo, oscillopsia (the visual illusion of movement of a stationary object due to spontaneous nystagmus), unilateral canal paresis with a positive head impulse test (HIT), nausea, vomiting, exacerbation of vertigo with head movement, and imbalance. Depending on the presence or absence of auditory symptoms, an APV is further classified as either labyrinthitis or vestibular neuritis, respectively. Vertigo is maximal within minutes to hours and can persist for days to weeks. There may be a viral prodrome or a history of brief vertiginous attacks in the days prior to the onset of prolonged vertigo.

Questions for consideration:
1. What is the pathophysiology of nystagmus?
2. How is the vestibular system assessed on physical examination?
SECTION 3
In an acute destructive lesion affecting 1 labyrinth, such as an APV, symptoms result from ipsilesional afferent hypoactivity and relative contralesional hyperactivity from the vestibulocochlear nerve. During a normal head turn to the left, there is left-greater-than-right asymmetry in afferent vestibular signals and the eyes drift to the right to maintain stable vision (i.e., vestibulo-ocular reflex or VOR). A right APV is perceived as a leftward head turn even though the head is still. As a result, the eyes continuously drift to the right (slow phase of nystagmus), and a position reset mechanism (fast phase) quickly brings the eyes back to the left (to midline) (figure 1). The nystagmus is of larger amplitude when gazing in the direction of the fast phase (i.e., Alexander law). The horizontal component of peripheral vestibular nystagmus is inhibited with fixation (there is a poor torsional fixation mechanism), which does not occur with central causes of vestibular nystagmus.

Since the intensity of peripheral nystagmus is influenced by fixation, observation under various conditions can help distinguish central vs peripheral causes of vertigo as peripheral nystagmus inhibits with fixation, and conversely, increases with fixation removed. Occlusive funduscopy is performed by visualizing the optic disc with an ophthalmoscope and then covering the patient’s viewing eye, thus removing fixation, which enhances peripheral nystagmus but has no effect on central nystagmus.

Similarly, the penlight cover test involves having the patient fixate on a penlight, and then covering 1 eye, thus removing fixation as the uncovered eye continues to view only the bright penlight. Having the patient view a featureless scene such as a piece of white paper has a similar effect: since there is no feature available for foveation, fixation is suppressed.

Dynamic assessment of the vestibular system includes the HIT, which tests angular VOR function (figure 2). Although a peripheral pattern of nystagmus with an abnormal HIT implies labyrinthine or vestibular nerve dysfunction, it is important to recognize that the etiology may be ischemia. The vascular supply to the inner ear is via the internal auditory artery, so a “peripheral” lesion can be from infarction.

Another important sign to look for in the AVS is a skew deviation, which is a nonparalytic premacular vertical ocular misalignment due to an imbalance of utricular inputs to the ocular motor system. It is often accompanied by features of the ocular tilt reaction (OTR), which includes the triad of skew deviation, head tilt, and ocular counterroll. A skew deviation is best demonstrated during alternate cover testing demonstrating vertical correction of the uncovered eye to maintain fixation, or subjectively with Maddox rod testing. A skew deviation and a fourth nerve palsy may present similarly (figure 3). A skew deviation occurs most

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**Figure 1** Pathophysiology of peripheral nystagmus in an acute peripheral vestibulopathy

Nystagmus from an acute peripheral vestibulopathy (APV) is mixed horizontal-torsional, indicating a lesion of the entire vestibular nerve or all semicircular canals within one labyrinth. Stimulation of individual canals move the eyes in distinct planes (i.e., horizontal, vertical, or torsional). In a right APV, the direction of nystagmus is determined by the intact left labyrinth: the 2 oppositely oriented left anterior and posterior canals cancel out vertical movement, leaving only a slight torsional component contributed from each, while the horizontal vector is attributable to the unopposed left horizontal canal. This generates a slow (pathologic) phase (in red) toward the affected ear with a fast (position reset) phase (in black) away from the affected ear. Nystagmus is named for the direction of the fast phase. The nystagmus is present in primary position and beats in the same direction (unidirectional) with gaze to either side. LAC = left anterior semicircular canal; LHC = left horizontal semicircular canal; LPC = left posterior semicircular canal; RAC = right anterior semicircular canal; RHC = right horizontal semicircular canal; RPC = right posterior semicircular canal. Redrawn and modified from Leigh RJ, Zee DS. The Neurology of Eye Movements (Contemporary Neurology Series), 4th ed. New York: Oxford University Press, Inc., 2006: figure 2-2. By permission of Oxford University Press, Inc.
commonly with brainstem or cerebellar lesions, but also may be seen with a lesion anywhere from the utricle to the interstitial nucleus of Cajal in the rostral midbrain.11

Other signs of central localization of acute vertigo include direction-changing (i.e., gaze-evoked or bidirectional) nystagmus, pure horizontal, torsional, or vertical nystagmus, impaired or asymmetric smooth pursuit, inability to suppress the VOR (combined eye-head tracking of moving targets), dysmetric saccades, and associated brainstem and long tract signs.12

In our patient, blood pressure was 143/79 mm Hg and general medical examination including otoscopy were normal. In primary gaze there was left-beating horizontal-torsional jerk nystagmus that intensified with left gaze, and lessened but remained left-beating in right gaze (video, first half, on the Neurology® Web site at www.neurology.org). The nystagmus intensified with removal of fixation during oculusive funduscopy and the penlight cover test. The HIT was normal to the left but abnormal to the right (video, second half), demonstrating a catch-up saccade, confirming a hypoac-
tive right VOR. Suppression of the VOR, smooth pursuit, and saccadic eye movements were normal. There was no vertical misalignment. When testing tandem gait, there were multiple side-steps to the right, and she could not maintain balance with Romberg testing. The remainder of the neurologic examination was normal.

Questions for consideration:
1. What are the most common manifestations of cerebellar ischemia?
2. What are the 3 most important bedside ocular motor tests to differentiate a stroke from an APV?
3. How has the examination narrowed the differential diagnosis in this patient?
### Table: Distinguishing peripheral vs central localization in the acute vestibular syndrome

<table>
<thead>
<tr>
<th>Clinical sign</th>
<th>Peripheral</th>
<th>Central</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nystagmus</td>
<td>Unidirectional; mixed horizontal-torsional; obeys Alexander’s law; slow phase with constant velocity; more intense when lying with affected ear down</td>
<td>May change direction; pure horizontal, torsional, or vertical; slow phase with constant, increasing or decreasing velocity</td>
<td>Peripheral nystagmus suppresses with fixation and increases with fixation removed, while central nystagmus is poorly suppressed by fixation[7]</td>
</tr>
<tr>
<td>Head impulse test (horizontal)</td>
<td>Abnormal</td>
<td>Typically normal</td>
<td>Lesions of the vestibular nucleus, root entry zone of 8th cranial nerve, or caudal cerebellum may cause an abnormal head impulse test[22]</td>
</tr>
<tr>
<td>Skew deviation</td>
<td>Absent</td>
<td>May be present</td>
<td>Rarely, a small skew may be apparent from a utricular lesion, but a large skew with diplopia suggests central localization[5]</td>
</tr>
<tr>
<td>Associated symptoms or signs</td>
<td>Hearing loss or tinnitus, minor gait instability, and veering toward the side of the lesion</td>
<td>Headache or neck pain (particularly concerning if abrupt onset, prolonged, or severe), weakness, numbness, diplopia, dysarthria, dysphonia, dysphagia, Horner sign, drop attack (abrupt fall with preserved level of consciousness), incoordination, marked gait instability, and atropulosis</td>
<td>A central lesion presents uncommonly as isolated vertigo</td>
</tr>
</tbody>
</table>

### SECTION 4

In a series of 66 patients with isolated cerebellar infarctions, vertigo and lateropulsion (defined as an irresistible sensation of falling to one side) were the most common symptoms.[7] Although vertigo and lateropulsion can each occur in isolation with a cerebellar stroke, other signs and symptoms are typically present, including limb ataxia, nausea/vomiting, truncal ataxia, dysarthria, nystagmus, headache, confusion, or somnolence.[5]

A stroke in the posterior inferior cerebellar artery territory can cause a “pseudovestibular neuritis” manifesting as isolated vertigo without auditory or other symptoms, but typically has a normal HIT.[5] A superior cerebellar artery stroke can cause a “pseudointoxication” picture because of gait or truncal ataxia with dysarthria, or “pseudogastroenteritis” with nausea and vomiting.

The internal auditory artery (IAA) is an end artery from the anterior inferior cerebellar artery (AICA) that supplies the vestibulocochlear nerve, cochlea, and vestibular labyrinth. Due to a paucity of collaterals, the IAA is vulnerable to ischemia. A labyrinthine infarction usually presents with sudden loss of hearing and vertigo accompanied by other AICA-territory signs (e.g., cerebellar, lateral pontine, or midbasilar syndromes).[2,5] However, isolated labyrinthine ischemia may herald AICA infarction.[2,10] In a series of 82 patients with AICA strokes, 80 had acute prolonged vertigo and vestibular dys-function of peripheral, central, or combined origin; 35 had acute prolonged vertigo with audiovestibular loss; 24 had acute prolonged vertigo without audiovestibular loss, while a selective loss of vestibular (4) or cochlear (3) function was much less common.[10] AICA strokes have also been referred to as “pseudolabyrinthitis.”[9]

In patients presenting with the acute vestibular syndrome, the combination of direction-changing nystagmus, skew deviation, and a normal HIT were more sensitive in detecting stroke than MRI (table).[4] A normal HIT strongly indicates a central process, but an abnormal HIT is a less reliable indicator of a peripheral lesion because of AVP mimics (i.e., ischemia of the vestibular nucleus, root entry zone of the eighth cranial nerve, or caudal cerebellum may cause an abnormal HIT).[12,14] In addition to the findings on bedside examination, vertigo due to cerebrovascular disease should be considered if any of the following factors are present: stroke risk factors, risk of vertebral artery dissection, abrupt onset, inability to ambulate, paucity of nausea and vomiting with marked gait instability or severe nausea and vomiting with little gait instability, or other accompanying central neurologic symptoms and signs.[3]

Our patient had a right AVP without auditory symptoms, and was diagnosed with vestibular neuritis. Prior to evaluation by the authors and within 24 hours of symptom onset, a brain MRI was found to be normal. Although brainstem/cerebellar infarctions may be missed acutely on MRI, the positive HIT, unidirectional nystagmus, and absent skew deviation all pointed away from a central process, and therefore an MRI was arguably unnecessary.[4] Her symptoms improved significantly over several days with only antiemetics, and vestibular rehabilitation was recommended.
General Submission Instructions

The Resident and Fellow Section is a primarily online feature that serves the resident and fellow readership. Residents and fellows are expected to be the primary authors for most submissions, but those highly involved in graduate medical education (e.g., program directors) may also contribute submissions on appropriate topics. Submissions for all article categories should be no more than 1,500 words; permission for longer articles will be needed from the editors. The number of references should be 10 or less and one to two tables or figures may be incorporated. The topic must be mentioned in the cover letter of the submission. Potential article topics include: teaching, ethics, practice, career choices, residency training, editorial, international education, research, historical, opinion, book review, training videos, or teaching NeuroImages. Teaching NeuroImages has the same requirements as NeuroImages but is especially valuable to the trainee audience and will be published in the online Resident and Fellow Section. Queries and comments should be addressed to Mitchell Elkind, MD, MS, FAAN, or Kathy Pieper at kpieper@neurology.org.
Clinical Reasoning:
A 33-year-old woman with severe postpartum occipital headaches

Figure 1  Head MRI axial cuts: Fluid-attenuated inversion recovery (FLAIR) (A, B, E, F) and apparent diffusion coefficient map (C, D, G, H) sequences

Upper panel MRI, performed on admission, showed FLAIR hyperintensities and diffusion restriction in the right parietal lobe and in the splenium of the corpus callosum (arrows). Lower panel, done on hospital day 3 when the patient deteriorated, showed worsening lesions involving the cortex and subcortical white matter of the parietal, posterior frontal, and occipital lobes, bilaterally (arrows).

SECTION 1
A 33-year-old woman with history of occasional “migraines” complained of severe occipital headache, following an uncomplicated full-term vaginal delivery under epidural anesthesia. This headache was qualitatively and quantitatively different from her usual headaches. The diagnosis of low intracranial pressure headache related to inadvertent dural puncture was considered and 2 epidural autologous blood patches were performed with no relief. One week postpartum she presented to an outside hospital with complaints of poor concentration, difficulty in finding words, getting dressed, and feeding herself, and left arm numbness. Examination showed a blood pressure of 179/119 mm Hg, poor attention span, apraxia, and decreased sensation in the left hand. General physical examination was unrevealing.

Head MRI (day 0) showed fluid-attenuated inversion recovery (FLAIR) hyperintensities (figure 1, A and B) and diffusion restriction with positive apparent diffusion coefficient (ADC) map (figure 1, C and D) in the right parietal lobe and in the splenium of the corpus callosum. The diagnosis of posterior reversible encephalopathy syndrome

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Disclosure: The authors report no disclosures.
(PRES) was entertained and the patient was treated for that condition with the antihypertensive agents nifedipine and lisinopril. The patient’s condition deteriorated. On the third hospital day, she became cortically blind and mute, and had motor perseverations and left-sided weakness. Repeat head MRI showed marked worsening with lesions involving the cortex and subcortical white matter of the parietal, posterior frontal, and occipital lobes, bilaterally (figure 1, bottom panel).

**Question for consideration:**
1. What is the differential diagnosis?

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**SECTION 2**

The differential diagnosis of multifocal infarcts in the distribution of many vascular territories is wide. It includes emboli from heart and aorta, disseminated intravascular coagulopathy, thrombotic thrombocytopenic purpura, moyamoya disease, vasculitis secondary to connective tissue and autoimmune systemic diseases, or viral/bacterial/fungal infections. Another possible rare entity is primary CNS angiitis. The presentation of this patient with postpartum headache, elevated blood pressure, and focal neurologic deficits suggested the diagnosis of PRES to the treating neurologist.

The sudden occurrence of severe headache in a young woman postpartum should also raise concern for sentinel headaches and subarachnoid hemorrhage because of their considerable morbidity and mortality and because they are eminently treatable if diagnosed early. These headaches are usually explosive, reach maximum intensity within minutes, and can last for hours to days. Subarachnoid hemorrhage is usually associated with symptoms and signs of meningeal irritation, altered consciousness, and focal neurologic signs. The presence of these signs in a peripartum woman should also raise the possibility of cerebral venous sinus thrombosis. Although these headaches commonly have a subacute onset, they might have a more acute presentation during puerperium. Pituitary apoplexy occurs as well in association with late pregnancy, presenting with acute headache, nausea, decreased visual acuity, ophthalmoplegia, and visual field defects.

**Question for consideration:**
1. What studies/tests should be performed?

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**SECTION 3**

In the outside hospital, head magnetic resonance (MR) venography was unrevealing. EEG showed mild diffuse slowing. Lumbar puncture yielded clear CSF that was acellular with normal glucose and protein content. Bacterial and fungal cultures, cryptococcal antigen, herpes simplex virus PCR, VDRL, and cytology were all negative.

Because of clinical deterioration, the patient was transferred to our university hospital where a head CT angiography (CTA) revealed segmental narrowing of many intracranial vessels but primarily involving the vertebral, basilar, posterior, and middle cerebral arteries (figure 2, A and B). Transcranial sonography measured increased flow velocities in right middle (170 cm/s), right posterior (230 cm/s), left middle (130 cm/s), and left posterior (140 cm/s) cerebral arteries. Vasculitis workup including erythrocyte sedimentation rate, C-reactive protein, rheumatoid factor, antinuclear antibody, anti-neutrophil cytoplasmic antibody, double-stranded DNA, anti-Scl/70, anti-SSA/Ro, anti-SSB/La antibodies, cryoglobulin, and angiotensin-converting enzyme was negative.

Based on the above, reversible cerebral vasoconstriction syndrome (RCVS) was suspected. The patient was treated with oral nimodipine, 60 mg every 4 hours; aspirin, 81 mg daily; and methylprednisolone, 125 mg IV every 6 hours for 6 days before the results of the vasculitis workup became available. The patient gradually improved; she became more alert but remained apathetic with partial expressive aphasia, apraxia, and perseveration. She perceived light and shades but her visual acuity remained below 20/200. She also had residual mild left hemiparesis with diffuse hyperreflexia and bilateral ankle clonus. Nimodipine was gradually tapered after 10 days and she was transferred to a rehabilitation facility.

Follow-up at 2 months after discharge showed her to be alert, with near-normal visual acuity (20/25) and intact color vision. She had residual right inferior quadrantanopia, apraxia, mild left hand weakness, and diffuse hyperreflexia. Head MRI showed evidence of encephalomalacia in the frontoparietal lobes, left occipital lobe, and splenium of the corpus callosum. Head MR angiography revealed complete
Figure 2  Head CT angiography (CTA) (A, B) and magnetic resonance angiography (MRA) (C, D)

Head CTA at day 6 reveals segmental narrowing of the left middle cerebral artery and the A1 segment of the right anterior cerebral artery (A, arrows); segmental narrowing of the posterior cerebral and left distal vertebral arteries with broad narrowing of the basilar artery (B, arrows). Head MRA 2 months after discharge shows complete reversal of arterial pathology (C and D). The magnification is similar in all parts of the figure; the white vertical band denotes 5 cm.

resolution of the previously noted vasoconstriction (figure 2, C and D).

DISCUSSION The most important information regarding the diagnosis and treatment of this patient was obtained before transfer to our hospital. The findings of positive diffusion-weighted imaging and ADC map in the right parietal lobe and splenium of the corpus callosum was indicative of ischemic stroke which is rarely seen in PRES.1 The clinical and MRI worsening after antihypertensive treatment makes the diagnosis of ischemic strokes more convincing. What is the cause of cerebral ischemia? She had no clinical evidence of heart disease. CTA ruled out moyamoya and premature atherosclerosis, and clearly revealed segmental narrowing of large and medium-sized arteries at the base of the brain, highly suggestive of RCVS.

RCVS refers to a group of disorders sharing angiographic and clinical features including reversible segmental and multifocal vasoconstriction of cerebral arteries, and sudden severe headaches with or without focal neurologic deficits or seizures. These disorders were previously reported as Call-Fleming syndrome, benign angiopathy of the nervous system, and postpartum angiopathy.2 The pathophysiology of RCVS remains unknown, though transient disturbance in the control of cerebral vascular tone was hypothesized.4

There is gender preponderance of RCVS in women. Half of the patients give history of migraine.2 The condition is idiopathic or related to a number of factors, including late pregnancy/postpartum and use of vasoactive substances such as triptans, selective serotonin reuptake inhibitors, pseudoephedrine, cannabinoids, cocaine, amphetamines, methylenedioxymethamphetamine (ecstasy), bromocriptine, and nasal decongestants.6 Postpartum angiopathy is an extremely rare complication that usually occurs in a normal pregnancy, as was the case in our patient. Two-thirds of those patients present in the first postpartum week.3 In 50%–70% of cases, it is associated with the use of vasoconstrictors, mostly ergots, to treat postpartum hemorrhage or to inhibit lactation. Intracranial hypotension, whether spontaneous6 or secondary to dural puncture,7 was also reported as a possible etiology of RCVS.

The diagnosis of RCVS is usually made on cerebral arterial imaging which shows diffuse and multifocal segmental narrowing of large and medium-sized arteries. The anterior and posterior brain circulations are involved. Occasional dilated segments, like strings and beads or sausage strings, were described. The diagnosis is confirmed only by documenting reversal of the vasoconstriction within few weeks.2

Vasoactive medications should be stopped. Clinical and angiographic resolution occurs spontaneously; however, calcium channel blockers like nimodipine are used with variable success. Long-term measures include secondary stroke prevention and treatment of complications.6–8 A short course of steroids may be justified to cover for cerebral vasculitis while awaiting results of workup, although a recent retrospective case-series study found worse outcome in patients who received steroids. However, this matter is confounded by the possibility that steroids were administered to sicker patients.9

The clinical outcome is usually good, with most patients recovering completely within days to weeks. The major complications of RCVS are localized cortical subarachnoid hemorrhages (20%–25% of cases) and ischemic strokes (5%–10%).9 Hemorrhagic complications and seizures occur earlier (within the first 10 days) compared to ischemic events (around 12 days from headache onset).2 Association with PRES10 and recurrence10 were reported.

Patients with severe new-onset headache and focal neurologic deficits must be assessed urgently and several diagnoses must be considered. Initial diagnostic
studies should include an unenhanced head CT and lumbar puncture. If both studies are normal, head MRI, MR angiography of the head and neck, and MR venography are necessary. When this workup reveals segmental vasoconstriction, normal or near normal CSF studies, and a lack of any other underlying pathology, RCVS should be considered. In the case we presented, PRES was initially suspected, so blood pressure was aggressively controlled, which worsened brain ischemia. Thus, antihypertensive agents should be used with caution in RCVS, just like any other condition causing ischemic strokes.

AUTHOR CONTRIBUTIONS
Dr.Maisouni: drafting/revising the manuscript, study concept or design, analysis or interpretation of data. Dr. Haik: drafting/revising the manuscript, study concept or design, analysis or interpretation of data.

REFERENCES
The Child Neurology Section in the Resident and Fellow Section of Neurology focuses on contemporary educational issues in child neurology. The goal of the section is to provide up-to-date reviews on important topics in child neurology that are relevant to all neurologists, both adult and child, particularly those still in their training. Examples include management of acute stroke in children, childhood demyelinating disease, neuroimaging in metabolic disorders, and the neurobiology of autism. Each piece will begin with a patient case, followed by a brief discussion about the differential diagnosis and a detailed discussion about the topic of focus. Submissions are welcome from residents and fellows in either child or adult neurology. Ideally, submissions will include the patient case as well as the discussion, but submission of timely review articles without an accompanying case will also be considered. In this situation, the editors of this section may supply an appropriate patient case.
Child Neurology: Paroxysmal stiffening, upward gaze, and hypotonia

Hallmarks of sepiapterin reductase deficiency

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M. Wagner, MD
A. Somerville, MD
B. Thöny, PhD
N. Blau, PhD
P. Weber, MD

Sepiapterin reductase deficiency (SRD) is a dopasensitive neurotransmitter disorder, caused by mutation of the SPR gene located on chromosome 2p14-p12. To date, 31 patients with 14 mutations have been diagnosed (BIODEF database, update November 2010, www.biopku.org).

While classic tetrahydrobipterin deficiencies present with hyperphenylalaninemia and deficiency of monoamine neurotransmitters, SRD is typically associated with normal phenylalanine levels in blood and pterins in urine and not detectable by neonatal screening for phenylketonuria. This implies how important it is to diagnose this condition clinically, in order to provide timely and proper treatment. A summary of the pathophysiology and biochemical pathway is provided by Bonafé et al.2

With the following case report and review of 21 published cases,2-10 we elucidate the clinical features of SRD as well as the diagnostic strategy and therapeutic approach.

CASE REPORT We present a 5-month-old girl, the first and only child born to consanguinous Turkish parents. The parents described the girl’s abnormal movements at 3 months of age as sudden stiffening of the whole body, extension of the extremities, upward gaze, and chewing movements lasting for several minutes often after meals, which we also could observe during her hospital stay. Pregnancy and delivery were uneventful. Birthweight, length, and head circumference were within normal ranges. During EEG, a few episodes with chewing movements could be recorded, but no epileptic discharges were evident. The brain MRI was unremarkable. We suspected gastroesophageal reflux and started therapy with omeprazole. The parents reported that the episodes diminished.

At 8 months of age, the patient was readmitted because the crises recurred with an increased frequency and duration of up to 25 minutes. During the episodes, the patient revealed circling movements of the hands and rhythmic tremor of the tongue in addition to the previously mentioned symptoms. Remarkably, the symptoms could be interrupted by voluntary movements. For example, the patient could promptly focus and precisely grab an interesting toy. Yet the abnormal movements resumed immediately when the object was taken away. During these episodes the patient stayed fully conscious, but seemed to be mildly disturbed. Interestingly, the episodes became more severe and lasted longer when the child had an infection or was under emotional stress.

Extensive diagnostic workup revealed an abnormal CSF neurotransmitter pattern with elevated levels of sepiapterin, 15.1 nmol/L (normal range: not detectable), and total bipterin 74 nmol/L (10–50 nmol/L), and low levels of 5-hydroxyindolacetic acid, 10.3 nmol/L (114–336 nmol/L), and homovanillic acid, 84 nmol/L (295–932 nmol/L), indicating a SRD. This could be confirmed by functional enzymatic fibroblast analysis in which the activity of sepiapterin reductase was not detectable (<0.1, normal range 99–185 μU/mg protein). Mutation analysis revealed a novel homozygous mutation in the SPR gene allele p.R219X in exon 3 (c.655C>T), resulting in an early stop codon, probably causing an inactive enzyme. In both parents, a heterozygote mutation was confirmed. They are related in both maternal and paternal lines, being concurrently first- and second-degree cousins.

The parents agreed to the patient’s treatment at the age of 11 months. We started therapy with 1-dopa/ benserazide (3.2 mg/kg/day) and 5-hydroxytryptophan (3 mg/kg/day), per or 4 times daily, which resulted in a complete cessation of the episodes 3 weeks after starting therapy. Our patient tolerated the therapy very well and never had any side effects. In the long term the administration 4 times daily was hardly feasible and resulted in sleep problems and substantial stress to both the child and the parents. Therefore, we extended the ad-
ministration to 3 times per day, at the age of 17 months, without any problems.

To date, our patient is developing within the normal range. At the age of 21 months, our patient has become a vivid girl with a strong will, who is very clingy to her mother. Worth mentioning are rather sweaty hands and feet, drooling, especially when the girl is focused, and behavioral issues with a tendency toward hyperactivity and distractibility.

**DISCUSSION AND REVIEW**

Diagnostic workup.
The diagnosis of SRD is straightforward via CSF analysis, showing a specific pattern: the levels of the pterins, in particular sepiapterin, are elevated, whereas the 5-hydroxyindolacetic acid and homovanillic acid concentrations are extremely low. This is a consistent finding also in our case.

Additional fibroblast analysis confirms the enzymatic inactivity of sepiapterin reductase. Mutation analysis of the patient and parents is helpful for genetic counseling.

**Symptoms.** Data were available in all cases. SRD causes symptoms which are related to a disturbed dopamine and serotonin metabolism such as dystonia, speech problems, hypersomnia, and neurocognitive deficits. The spectrum of symptoms is listed in figure 1.

Particular symptoms seem to be age specific. The triad upward gaze (often described as oculogyric crises in previous reports), paroxysmal stiffening, and hypotonia tend to occur early in infancy as one of the first symptoms, which was also the case in our patient, and should be defined as early clinical hallmarks of SRD. Other symptoms requiring higher motor skills and coordination, such as ataxia and dysarthria, can be seen in later course. In adolescents and adults, hypersomnia seems to be one of the main complaints, next to dystonia. Figure 2 summarizes the age-related clinical hallmarks of SRD.

One interesting finding, which has not been reported previously, was the interruptability of the symptoms by voluntary movements. This phenomenon can perhaps be explained by the fact that the girl was still young and probably did not yet have significant neuronal damage. We do not have an explanation why, in a few cases, some symptoms like oculogyric crises disappear spontaneously in later course.

**Therapy.** The therapy strategy is straightforward by substituting both precursor substances l-dopa and 5-hydroxytryptophan, enabling a normalization of the CSF profile.
The combination therapy is assumed to be the optimal therapeutic strategy, but it has to be noted, especially since 5-hydroxytryptophan is not available everywhere.

Most patients seem to respond to a combination therapy with L-dopa and 5-hydroxytryptophan. Since some patients might easily get side effects, we recommend a very low starting dosage of about 0.5 to 2 mg/kg/day. Because of the short half-life period of L-dopa, the ideal application rate would be at least 3 times daily. For follow-up, the analysis of prolactin levels in serum has shown to be a useful surrogate parameter for dopamine metabolism, if it was elevated prior to therapy.3,9

**Neurodevelopmental outcome.** To date, our patient is developing well within normal range. Though we observe a certain hyperactivity and distractibility, at this time it is very difficult to interpret and too early to try to define the neuropsychological profile of affected individuals.

In 18/21 previously reported cases, treatment with L-dopa alone or with 5-hydroxytryptophan did not have any significant influence on cognitive performance.2–10 The cognitive impairment ranges were defined as mild to severe, with an IQ ranging between 36 and 60 in 4 tested cases.6,8,10 There are only 2 patients who received treatment under 1 year of age. The first patient from Malta did not show an improvement in cognitive performance.7 For the other patient from India there were no data regarding the cognitive outcome.10 Three of 21 cases, 2 Greek siblings3 and 1 Dutch patient,9 had minor cognitive delay prior to treatment with L-dopa and were able to attend normal school in later course upon treatment.3

SRD shows specific clinical findings which may present in infancy as the triad of paroxysmal freezing, upward gaze, and hypotonia. Later, childhood and adulthood dystonia with hypersomnia and ataxia may be striking. A combination therapy with L-dopa and 5-hydroxytryptophan improves the motor symptoms significantly in the majority of cases. The cognitive skills seem to be less influenceable if the patients already show significant neurocognitive impairment.

This highlights the importance of early diagnosis and treatment of this disorder as there is a chance of a normal developmental outcome.

**AUTHOR CONTRIBUTIONS**

Dr. Dill: drafting/revising the manuscript, analysis or interpretation of data, acquisition of data. Dr. Wagner: drafting/revising the manuscript, study concept or design, analysis or interpretation of data, acquisition of data. Dr. Somerville: study concept or design, analysis or interpretation of data, acquisition of data. Dr. Thöny: analysis or interpretation of data, contribution of vital reagents/materials/patients, acquisition of data, study su-
pervision. Dr. Blau: drafting/revising the manuscript, study concept or design, analysis or interpretation of data. Dr. Weber: drafting/revising the manuscript, study concept or design, analysis or interpretation of data.

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DISCLOSURE
Dr. DB, Dr. Wagner, Dr. Somerville, and Dr. Thony report no disclosures. Dr. Blau serves on a scientific advisory board for and receives research support from Merck Serono and serves on the editorial board of Molecular Genetics and Metabolism and as Communicating Editor for the Journal of Inherited Metabolic Disease. Dr. Weber serves on a scientific advisory board for Eli Lilly and Company; has received funding for travel or speaker honoraria from Eli Lilly and Company and Pfizer Inc.; serves on the editorial boards of Arzneimittel Forschung and Pflügers Archiv; and receives research support from Mepha (Teva Pharmaceuticals Industries, Ltd.), Swiss National Foundation, Marie-Anna-Stiftung, and Stiftung für den kranken Kind.

REFERENCES
EMERGING SUBSPECIALTIES IN NEUROLOGY

These manuscripts will review the history and development of emerging subspecialties in neurology, including fields such as Pain Medicine, Headache, Neurocritical Care, Interventional Neurology, and others. The focus should be on educating residents with a possible interest in this subspecialty. Those interested in writing these manuscripts should contact the Resident and Fellow Section Editor before submission to inquire about the need for an article on a particular topic.
Autoimmune and immune-mediated mechanisms are increasingly appreciated in many neurologic diseases. The goal of fellowship training is to develop an understanding of the pathophysiology and treatment of these diseases with a focus on immunology that is not traditionally afforded to most trainees during residency or fellowship. Neuroimmunology is an expanding subspecialty with rapidly emerging developments from the clinical and basic sciences necessitating frequent change in clinical practice. Historically, the first international congress of neuroimmunology was held in 1982, with the actual founding of the International Society of Neuroimmunology not occurring until after the second international congress in 1987. The origins of neuroimmunology, however, pre-date the establishment of the society by nearly a century, and modern clinical neuroimmunology has its roots in the interdisciplinary collaboration of neurologists, pathologists, internists, and other specialists in the early 1950s. The field of neuroimmunology intersects many traditional neurology subspecialties, including diseases within epilepsy, movement disorders, neuromuscular, autonomic neurology, neuro-oncology, behavioral neurology, degenerative disorders, and demyelinating diseases.

Training programs in neuroimmunology focus on autoimmune and immune-mediated diseases, with attention to the contribution of immune system–based mechanisms to the neurologic manifestations. Training also focuses on the pharmacologic and treatment implications of these diseases. Within neuroimmunologic disease, multiple sclerosis (MS) is perhaps the most prominently studied disease, likely owing to its prevalence and the early recognition of the role of the immune system in the pathophysiology of MS. Despite its prominence, however, it is only one of many neuroimmunologic diseases.

**TRAINING OPPORTUNITIES IN NEUROIMMUNOLOGY** There are currently no Accreditation Council for Graduate Medical Education–supported fellowships for neuroimmunology, autoimmune neurology, or MS and related diseases. This has funding implications, as some programs may strongly encourage or require the fellow to identify funding for his or her fellowship. In addition, there is presently no board examination and no specific diploma is issued at the end of the fellowship. Non-accredited subspecialty fellowship training is currently available in this field at several institutions.

The amount of time devoted to patient care, basic science research, or clinical research varies considerably between programs. Some neuroimmunology fellowship training programs essentially focus solely on MS, with other programs having variable amounts of exposure to MS as a part of a more comprehensive immunology approach. Successful training in neuroimmunology, as in any subspecialty, greatly benefits from mentorship with an expert in the field.

Individual programs vary widely in the availability of training in the management of the neurologic manifestations of rheumatologic diseases. Similarly, exposure to paraneoplastic syndromes with either peripheral or CNS manifestations varies widely between institutions. Trainees with a special interest in these diseases should specifically query each program to determine the institutional approach to the interdisciplinary management of such patients, estimated patient volume, and mentor expertise. Additionally, some institutions may offer training to further subspecialize by combining fellowships. The addition of neuroimmunology training to more traditional fellowship tracks would allow the trainee a unique perspective to approach the emerging and increasingly recognized associations of neuroimmunology with a variety of neurologic conditions, including autoimmune dementia, epilepsy, and nerve and muscle disease, as well as the neurologic complications of rheumatologic diseases such as systemic lupus erythematosus, Sjögren syndrome, and thyroid disease. For example, a neuroimmunology fellowship could be preceded or followed by a neuromuscular fellowship with the goal of specializing in immune-mediated/paraneoplastic disorders of the peripheral nervous system. Alternatively, epilepsy fellowship training in addition to training in neuroimmunology would allow for specialization in autoimmune epilepsy.

An alternative training path to a neuroimmunology fellowship could be a customized experience establishing joint training with rheumatology and clinical immunology services; this approach would rely on a strong mentor.

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Go to Neurology.org for full disclosures. Disclosures deemed relevant by the author, if any, are provided at the end of this article.
The National Multiple Sclerosis Society sponsors several different types of clinical and research fellowship awards, contingent upon the applicant making arrangements with an appropriate mentor and sponsoring institution prior to application. Award types are listed in Table 1 and additional information can be found at www.nationalMSsociety.org/fellowships. This funding mechanism can be utilized to fund a position in an established fellowship program, or to create an individualized fellowship at a supportive institution. As described in the criteria in Table 1, these fellowship awards necessarily have an MS focus.

The Veterans Administration (VA) offers 1- to 3-year fellowships in MS and neuroimmunology at the VA MS Centers of Excellence. The fellowships are offered affiliated with the VA Centers of Excellence, with locations in 3 states: Washington (Seattle), Oregon (Portland), and Maryland (Baltimore). Fellows have the opportunity to customize training to obtain skills in clinical, scientific, and applied therapies for MS. More information is available at http://www.va.gov/oaa/.

Given the scope and variety of neuroimmunology programs, it can be challenging to attain a comprehensive overview of available training opportunities. There is no clearinghouse of all neuroimmunology/autoimmune neurology fellowships, and thus the prospective trainee should consider proactively approaching his or her ideal fellowship by identifying a mentor or contact person within the field, and discussing potential career goals within neuroimmunology. Internet searches directed toward “neuroimmunology fellowship,” “autoimmune neurology,” and “MS fellowship” yield several leads on prominent programs. Table 2 provides a sample of available fellowships in neuroimmunology, representing the results of a Google Internet search (January 30, 2012) for “Neuroimmunology Fellowships.” The table lists all programs returned utilizing these search terms, inclusive of the top 100 results. Program directors were sent an e-mail query to verify the accuracy of the information on the fellowships. Please note that this list is not inclusive of all neuroimmunology fellowships available, but is provided to represent the breadth of programs demonstrated by performing a basic Internet search. Also, many institutions do not specifically promote a neuroimmunology or MS fellowship, but create positions for qualified candidates.

This approach, coupled with contacting specific individuals within institutions based on an applicant’s desired location, is a reasonable one. Given that many fellowships prefer trainees to apply for funding, applicants will likely need at least 18 months of lead time in contacting and applying to programs to allow for interviews, program selection, and identification of funding opportunities. Many programs have a rolling admission process, while others have a strict application deadline extending as far as 18 months prior to matriculation.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Fellowships offered through The National Multiple Sclerosis Society*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Criteria</strong></td>
<td><strong>Details</strong></td>
</tr>
<tr>
<td>Clinical Care Physician Fellowship</td>
<td>Mentored postresidency training in specialized multidisciplinary MS clinical care for US-licensed neurologists 1-year award; $65,000 for salary, fringe, administrative</td>
</tr>
<tr>
<td>Sylvia Lawry Physician Fellowship</td>
<td>Mentored postresidency training in the design and conduct of MS clinical trials for board-eligible/certified neurologists licensed in the United States Formal coursework in clinical research included in training; 2- to 3-year award; $65,000/year for salary, fringe, tuition</td>
</tr>
<tr>
<td>National MS Society–American Academy of Neurology MS Clinician Scientist Development Award</td>
<td>Mentored training for postresidency physicians committed to a career in academic MS clinical research Open to PGY 4 and 5 residents/fellows licensed in the United States; 3-year award; $75,000/year for salary plus institutional allowance</td>
</tr>
<tr>
<td>Postdoctoral Fellowship</td>
<td>Mentored training for MD or PhD postdoctoral fellows for MS-related research projects in basic science, clinical, or patient management, care, and rehabilitation topics Open to individuals with 0–36 months of postdoctoral training; 1- to 3-year award; salary plus institutional allowance</td>
</tr>
<tr>
<td>Career Transition Award</td>
<td>Provides 2 years of mentored advanced postdoctoral training and 3 years of faculty support for MDs or PhDs pursuing research projects in MS Open to individuals with 2-5 years of previous postdoctoral training; salary and $25,000/year research allowance for postdoctoral phase; $125,000/year in direct costs for faculty phase</td>
</tr>
</tbody>
</table>

Abbreviation: MS = multiple sclerosis.
* This table was adapted from the MS Society Web site with only minor changes.
Table 2  Sample of available fellowships in neuroimmunology, representing the compiled results of a Google Internet search (January 30, 2012) for “Neuroimmunology Fellowships”*

<table>
<thead>
<tr>
<th>Institution</th>
<th>Years of training</th>
<th>Program description and focus, derived from program Web site</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cleveland Clinic: Clinical Neuroimmunology Fellowship</td>
<td>1-3</td>
<td>Academically oriented neurologists to pursue a career in patient care and clinical research in MS and related disorders.</td>
</tr>
<tr>
<td>Johns Hopkins University: Neuroimmunology &amp; Neurological Infections Fellowship Program</td>
<td>2+</td>
<td>Pursue careers in academic medicine as independent clinician investigators either solely in the clinic or with laboratory research.</td>
</tr>
<tr>
<td>Mayo Clinic: Autoimmune Neurology and MS Fellowships</td>
<td>1-2</td>
<td>1) Autoimmune Neurology Fellowship: combines diagnosis/management of idiopathic and paraneoplastic disorders with contemporary immunologic concepts. The program complements many subspecialties [neuromuscular, autonomic/PNS, inflammatory and demyelinating CNS disorders, behavioral/cognitive, movement and seizure disorders]. Abundant opportunities for translational/clinical research and optional rotations. Prepares trainees to pursue a career in academic neurology, tailored to fellow's goals. 1) MS Fellowship: combines clinical and research experience with exposure to a spectrum of adult and pediatric demyelinating diseases. Fellows are expected to spend 50% of time in research and 50% of time in the clinic.</td>
</tr>
<tr>
<td>NIH: Neuroimmunological Diseases Unit</td>
<td>2+</td>
<td>Geared to applicants interested in career of physician-scientist; it combines clinical training in immunology with extensive research experience.</td>
</tr>
<tr>
<td>St. Joseph’s Hospital and Medical Center/Barrow Neurological Institute: Neuro-Immunology Fellowship Program</td>
<td>1-2</td>
<td>The first year focuses on the clinical and clinical research program, developing the skills necessary to diagnose, treat, manage, and conduct clinical research; if desired, the fellow can develop a focused laboratory experience beginning in the second year of the fellowship, or pursue research in the clinical and neuroimaging arenas.</td>
</tr>
<tr>
<td>University of Alabama: Neuroimmunology/MS Fellowship</td>
<td>2</td>
<td>The fellowship combines clinical patient care and investigation in an environment that has immunopathogenesis of demyelinating disease as its principal focus.</td>
</tr>
<tr>
<td>University of California San Francisco: Clinical Research Fellowships in MS</td>
<td>1-3</td>
<td>Offers either clinical- or research-focused fellowships: the clinical fellowship is 1–2 years, allows for multidisciplinary exposure to clinical MS and related diseases through the adult and pediatric MS clinic; research-focused fellowships can be oriented either toward clinical research or basic research, duration is 2–3 years developing research projects under the mentorship of MS center faculty and seeing patients in clinic.</td>
</tr>
<tr>
<td>University of Maryland: Fellowship training program in Neuroimmunology at the Maryland Center for MS</td>
<td>2+</td>
<td>The program enables trainees to become independent investigators in the conduct of basic and clinical research in the broad field of MS.</td>
</tr>
<tr>
<td>University of Massachusetts: Fellowship in Neuroimmunology</td>
<td>1-2</td>
<td>Intensive clinical training in MS, and design and implementation of clinical trials.</td>
</tr>
<tr>
<td>University of North Carolina: Neuroimmunology/MS Clinical Fellowship</td>
<td>1+</td>
<td>Provides a comprehensive training in clinical care, and in conducting clinical trials for patients with MS.</td>
</tr>
<tr>
<td>University of Texas Southwestern: MS Fellowship Program</td>
<td>1</td>
<td>Comprehensive training in the clinical evaluation and management of the patient with MS and related disorders.</td>
</tr>
<tr>
<td>University of Washington: MS &amp; Neuroimmunology Fellowships</td>
<td>1</td>
<td>Clinical fellowship in MS rehabilitation, emphasizes rehabilitative care in a clinical setting.</td>
</tr>
<tr>
<td>Vanderbilt University: Neuroimmunology Fellowship</td>
<td>1-2</td>
<td>Train physicians for careers in clinical therapeutics as pertains to MS and neuroimmunologic diseases.</td>
</tr>
<tr>
<td>Washington University, St. Louis: Neuroimmunology Clinical and Basic Research Fellowships</td>
<td>2-3</td>
<td>Two fellowship types (or hybrids) are available to selected neurologists and PhD scientists, to equip them for an academic career with emphasis on MS. 1) clinical, with formal training in biostatistics, clinical trial design, and ethics of human research, and the opportunity to obtain Master of Science in Clinical Investigation degree. 2) basic research in neuroimmunology.</td>
</tr>
</tbody>
</table>

Abbreviations: MS = multiple sclerosis; PNS = peripheral nervous system.

* The top 100 search results were reviewed, and results were excluded if they did not link to or directly refer to a fellowship program.

ACKNOWLEDGMENT
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DISCLOSURE
S. Carly serves as a member of the Editorial Board of the Resident & Fellow section of Neurology®. Go to Neurology.org for full disclosures.

REFERENCES

subspecialty autoimmune neurology or neuroimmunology clinic could be run independently or in conjunction with an MS clinic. An important role in the outpatient setting is the diagnosis and management of chronic immune-mediated or autoimmune disorders affecting the nervous system, as well as the differentiation of these disorders from disease mimics.

There are numerous opportunities to focus on MS and related diseases in private practice, and an MS-focused, clinically oriented fellowship would provide additional expertise in the treatment of this patient population. In private practice, a more plausible arrangement may be an MS specialty clinic in addition to general practice.
INTERNATIONAL ISSUES

More than 85 percent of the world's population lives in low- and middle-income countries, where the burden of neurologic disease is the largest. Relatively little is known, however, about patients and practitioners of neurology in most countries. This section aims to explore international issues in neurology education. We welcome manuscripts describing international educational exchanges, personal rotations and experiences in low- and middle-income countries, and work by neurology trainees from around the globe. Descriptions of notable differences in training between countries are of interest. Inclusion of practical information regarding how interested residents might get involved in international programs would also be of use.
International Issues: Neurology mission in the Ecuadorian Amazon rainforest

The article “An epileptologist brings EEG to the Ecuadorian Amazon jungle” in the December 2009 issue of Neurology Today caught Dr. Laccheo’s attention. She contacted Dr. Espinosa, an Ecuadorian neurologist trained in neuropsychology and epilepsy in the United States. Dr. Espinosa chairs a nonprofit organization providing free health care in Quito, and he leads a mission to provide health care in rural Ecuador. We participated in providing neurologic services to an underserved population in rural Ecuador in April 2011 during Dr. Laccheo’s last year of residency.

Ecuador ranked 97th among 175 countries in the world according to the United Nations’ Human Development Index in 2003—the second to last in South America. Thirty-one percent of the population lives in extreme poverty, with an income of less than 1 dollar per day. In the Amazon region, 66% lack access to a sewage system and 44% to electricity. Up to 50% of children under age 6 suffer from malnutrition and the mortality rate of children under 5 is 24/1,000.1 Thirty percent of the population lacks regular access to health services and two-thirds have no health insurance. Indigenous ethnicity is a strong predictor for less frequent use of health care services in Ecuador.2

Our neurology mission took place in Tena, located in a rural Amazon rainforest region east of the Andes Mountains at the junction of the Rio Tena and Rio Paño, about 200 km (5 hours drive) away from the capital, Quito (figure). Tena has a population of 45,000 that is mostly derived from the descendants of those who fled the Spanish invasion in the Andes in the 16th century. The thick rainforest is home to many natives and remains isolated from the rest of Ecuador with limited access to major cities and health care. The local hospital of Tena, Jose Maria Velasco Ibarra, has a 120-bed capacity and is the largest hospital in Napo province. Neurologic services are unavailable despite its large population, and there is no intensive care unit at the hospital. Critically ill patients are transferred to the major hospitals in Quito; however, without the availability of transportation by air, the 5-hour ambulance drive is a life-threatening challenge to those with major neurologic emergencies. Next to the hospital is PediHabilidad, the only rehabilitation clinic for children with disabilities in Napo province, founded in 2006 by an American trained physical therapist, Nicole Falcone. It started with 6 children with cerebral palsy and has grown to providing free rehabilitation services for over 400 children. It was Ms. Falcone who approached Dr. Espinosa to provide neurologic consultations to her patients, and this led to the first Neurological Brigade in April 2009. April 2011 was the third neurology brigade to Tena, bringing a total of 19 volunteers from the United States, including staff neurologists, a neurosurgeon, EEG technicians, various support staff, and the authors.

Data from the first mission in 2009 showed that 36% of patients had epilepsy (147 out of 475), though only 10 patients underwent neurologic imaging. A total of 101 patients were newly diagnosed with epilepsy, 42 patients had not received treatment for their epilepsy, and 71 patients were on inappropriate therapy. The calculated epilepsy treatment gap (patients evaluated with epilepsy not receiving treatment) was estimated to be 77%–80%, although the true gap may be larger in the community if one considers referral bias.3 A total of 1,078 neurologic consultations were seen (table), and 221 EEGs were performed during 3 annual medical missions combined. The rate of abnormal EEG findings in the epilepsy patients was 65% (epileptiform discharges and focal slowing), which seems to be higher than what we typically find in developed countries.4 Our higher rate of abnormal EEGs may be explained by referral bias, lack of neurologists in the area, and, more importantly, because epilepsy and EEG abnormalities are more prevalent in the developing world.5

In Tena, carbamazepine is most frequently used (>45%), followed by valproic acid (35%), and then

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Disclosure: Author disclosures are provided at the end of the article.
The red dot indicates the location of Tena, where the neurologic missions take place. Map modified from the CIA World Fact Book, available at https://www.cia.gov/library/publications/the-world-factbook/.

phenytoin (10%). Phenobarbital, which is widely used in other developing countries, is used in only 5% of epilepsy patients because phenobarbital is considered a controlled substance in Ecuador requiring a special prescription. According to a statement by the World Health Organization, in conjunction with the International League Against Epilepsy and International Bureau for Epilepsy, globally up to 85% of people with epilepsy are either inappropriately treated or not treated at all. Increased epilepsy rates in Ecuador may be partly attributed to parasitic and other infectious diseases as well as poor perinatal care. The mortality rate due to epilepsy may be as much as 3 times greater in the developing world (6.3 in Ecuador as compared to 2.1 in Rochester, MN).7

Our outpatient neurologic consultations took place using clinic rooms at Hospital Jose Maria Velasco Ibarra. Patients were mostly Native Indians (Quichuan) from remote villages, who often walked or canoed 3 hours, sometimes carrying their disabled child in a sling to seek medical care in Tena. Even the elderly often had to be carried on family members’ shoulders in order to reach the clinic. In one representative case, a mother brought a 1-year-old girl wrapped in a sling. She was born underweight and had multiple convulsive episodes starting at 6 months of age, though no diagnostic evaluation had been done and she was not being treated with anticonvulsants. She was flaccid except for facial twitching. An EEG confirmed she was having intermittent rhythmic bursts of high-amplitude anterior predominant 3-Hz spike and slow wave discharges. Because perinatal screening was not routinely available in Ecuador, concern was high for a potential reversible metabolic cause. Another mother entered the examination room tearful that the shaman was unable to cure her daughter’s spells of unresponsiveness and staring, and that she was no longer able to attend school. EEG confirmed absence epilepsy. As we explained the diagnosis, treatment, and prognosis, the mother again cried and shook my hands repeatedly, saying “muchas gracias”—I had never been appreciated this much before.

It appeared to me that there is also social stigma to neurologic disease in Ecuador that may contribute to the medical treatment gap—neurologic disease can be perceived as “mental illness” or a “spiritual problem.” Seeking cures by traditional remedies and rituals administered by the local shaman appears to be a common practice. Seizures can be seen as an attack of hysteria or possession by devils and are treated by beating with ortiga, a poison ivy–like plant, as a punishment. Children with physical impairments may be offered treatments in the form of massage with snake oils or cleansing using eggs, with the aim that this will cure or cure the impairment. Sadly, children with motor or cognitive deficits do not attend school and are isolated from the rest of society. Also, this society has little ability to adapt to children with developmental disabilities, due to a lack of assistive devices such as wheelchairs.

Much of our work involved not only offering medical diagnoses and treatments but also raising public awareness of neurologic disease. We participated in local and national television interviews and addressed the need for neurologic care in rural Amazon areas. We held neurologic seminars for local health care providers to educate them in the recognition and management of common neurologic conditions such as epilepsy, hydrocephalus, and cerebral
palsy. We worked closely with local internists and pediatrics so that continuity of care for the patients could be provided effectively after the US volunteers leave. Dr. Espinosa travels periodically to Tena, and also provides teleconsultations and e-mail consultations with local primary care physicians between annual brigades. The neurology mission of Tena is a model for other developing countries where access to neurologic care in remote areas is not available. As a resident, I was able to learn how to best treat patients with limited resources, and I began to appreciate how fortunate I am to provide care in a high-resource country.

On my last day in Ecuador, I visited the Museo Fundacion Guayasamin in Quito. Oswaldo Guayasamin was a 20th-century Ecuadorian sculptor and painter. His mother was mestizo (mixed heritage) and his father was indigenous. “Guayasamin” means “white flying bird” in Quichuan, an indigenous language of the Andes. He experienced the struggles of underprivileged indigenous people. His work is dedicated to social and political awareness of his people who have been ignored and exploited. The paintings portray faces of sadness and agony illustrated with strongly contrasting colors. Among his paintings, “Madre y Niño,” depicting a feeling of tenderness and affection of a mother and child despite adversity, reminded me of many patients and families I saw in Tena. An inscription in the museum stated “Yo lloro porque no tenía zapatos, hasta que vi un niño que no tenía pies” (“I cried because I had no shoes, until I saw a child with no feet”). The truth of this statement is difficult to realize until you see with your own eyes the difficulties faced by the people of Tena.

Trainees who wish to obtain more information about this program and opportunities to get involved should contact Patricio S. Espinosa, MD, MPH; e-mail: ps.espinosa@cien-ecuador.org; Internet: www.cien-ecuador.org.

AUTHOR CONTRIBUTIONS
Dr. Lacbeco drafted the manuscript. Dr. Espinosa revised and edited the manuscript.

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REFERENCES
RIGHT BRAIN

Right Brain is a feature devoted to the relationship between neurology and the medical humanities, with submissions either written by trainees or with a focus on the experience of the trainee. Appropriate submissions include articles, commentaries, and reflections on the interaction between neurology and history, literature, ethics, theology, sociology, anthropology, philosophy, poetry, theater, film, fine arts, or the media. Right Brain also will publish original works of fiction, poetry, and reflection written by residents and fellows relating to the practice of neurology or neurology training.
Right Brain:
A descriptive account of two patients’ experience with and adaptations to Bálint syndrome

We provide a narrative account of 2 patients’ experiences with Bálint syndrome, a rare and debilitating neurologic disorder characterized by optic ataxia, ocular apraxia, and simultanagnosia.

It was a quiet Thursday afternoon when A.S., a 68-year-old woman from a suburb of Chicago, awakened from a nap to the realization that something was terribly wrong. “I went to lie down, and when I got up, I couldn’t find where the cabinets were, or the doors,” she remembers. Over the next 2 days, A.S.’s confusion heightened as she increasingly lost her ability to name or even distinguish household objects that she’d been surrounded by for years. Unable to read the numbers on her telephone or to see where the bedroom wall ended and the bedroom door began, A.S. naturally thought that there was something wrong with her eyes and made an appointment with the ophthalmologist later in the week. She then did what so many stroke victims do; she put herself to bed early, hoping that everything would be better in the morning.

When the meeting finally came, it became clear that whatever A.S. was afflicted with, it was not a simple matter of visual impairment. “We took her to an eye doctor, because we didn’t know what it was at the time,” recalls her husband, Michael. “They ran tests on her eyes, and she passed them with flying colors!” A.S.’s visual acuity test tells the same tale; her vision tested out at 20/30 in each eye, and when she put on her glasses, it rose to 20/20. A.S. and her husband left the doctor’s office with normal examination results and a neurologic referral in hand, wondering what sort of ailment could rob her of her ability to see the bathroom sink while leaving her with what we typically think of as perfect vision.

At 66 years old, J.D. was a robust and active man, who was described by those who knew him as a workaholic who could not sit still. After emigrating to the United States from the former Soviet Union, where he had been mayor of a large town, J.D. began his quest for the American Dream as a truck driver. Fast-forward 30 years and he is again a pillar of his community, where he was heading a large extended family while owning and operating his own trucking business.

J.D. was often on the road for long hours, and so his family thought little of it when he began swerving erratically on the long drive to his son’s house for Thanksgiving dinner. “He worked double shifts for all 3 days before Thanksgiving because his workers wanted them off,” his daughter recalls. “We just thought he was tired.” Nor did his family know what to make of his bizarre attempts to serve himself at the table. “He was holding the spoon upside down. We all laughed,” she recalls.

What happened next was no laughing matter, as J.D. began to experience left-sided weakness, facial drooping, and eventually a loss of consciousness that caused his family to rush him to the emergency room. That scene at the table is his last memory of the 2 months that followed. During that time, J.D. remained unconscious and confined to bed, until suddenly and unexpectedly awakening one afternoon and deciding that it was time to get up and stretch his legs. Since then, his road to partial recovery of powers of speech and the use of his left extremities has been a slow one.

The stories of A.S. and J.D. appear dissimilar at first glance, but they are in fact both descriptions of the onset of a rare neurologic disorder known as Bálint syndrome. Bálint syndrome is generally caused by one or more ischemic strokes to the parietal and occipital cortices. Magnetic resonance (MR) studies showed that A.S. had had a series of cardioembolic infarcts involving the parietal and occipital cortices, bilaterally (figure, A). J.D. probably had a series of ischemic infarctions due to severe atherosclerotic vertebralbasilar disease (figure, B).

The resulting syndrome is characterized by a triad of symptoms: 1) oculomotor apraxia (difficulty initiating voluntary eye movements toward an object), 2) optic ataxia (inability to reach for objects under visual guidance), and 3) visual simultanagnosia (construction of the visual attentional field). Every neurology resident will have been acquainted with this syndrome, but to truly understand the Bálint
patient is to witness the devastating effect that these deficits have on ability to function.

A.D. begins her day as we all do, by attending to her hygiene. However, because of her profound oculomotor apraxia, she cannot judge her location relative to the bathroom sink, mirror, and walls by sight, but only through the guidance of her other senses. Accordingly, she has learned that she must touch the sink at all times in order to remain oriented—otherwise her eyes are as good as closed. Likewise, during her daily shower, she must keep her hand on the shower bar at all times. She once failed to do this, misplaced her foot, fell, and broke 2 vertebrae. "Now I’m afraid of falling all the time," she relates, adding that while she’s walking, the tension that accompanies this fear can be more exhausting than the act of walking itself.

Having showered and toweled off with some difficulty, A.S. explains how, because she cannot trust her eyes to direct the toothpaste to her toothbrush, she must put the toothpaste directly in her mouth, and by trial and error move the toothbrush to meet it. At breakfast she uses her hands for most everything, and cannot eat soup at all. Nor is tidying up after herself any easier, as is evident from A.S.’s account of her attempt to pick a pen up off the floor: "I see it, and when I go to pick it up, it’s not there! I was aiming for the pen, and I see it, but I can’t pick it up!"

Because J.D.’s strokes are more recent and more extensive, his word-finding ability has not improved as much as A.S.’s has. During examination, his wife’s presence is immensely helpful to him; she conveys his meaning, alleviating the frustration that his expressive aphasia causes. The biggest obstacles for J.D. to surmount in his morning routine are dressing and brushing his teeth. While he has no difficulty removing articles of clothing, putting them on is an adventure: "I can’t find the front and the back—it’s all mixed up!" he exclaims.

Nor are his activities of daily living all that have been affected. Once an avid reader, J.D. can no longer direct his eyes to scan a line of text. Moreover, when asked to read a written word aloud, J.D. might only see one letter of it, or even just one line from that letter, depending upon the distance at which it is held from his face. This is because, as part of his simultanagnosia, J.D. is only able to consciously attend to objects placed within a tiny window of his visual field at any given time.

For J.D., another result of the stroke that caused his Bálint syndrome has been depression. "I was never sad like this before," he said, and his wife confirms it. "He never once cried before, but now he cries often." J.D. is having trouble adjusting to a life in which he cannot work to provide for his family as he once did, but rather requires significant assistance in performing simple tasks. "I think that’s the worst part for him because he’s a man with a lot of pride who worked all his life, and now he can’t do anything," his daughter tells us.

Adaptation is key to recovered function in these patients. A.S. still finds a number of ways to enjoy herself. "The Library of Congress sends me audio books, and I can listen to the books anytime I want. They also sent me a radio so that I can listen to the news, because I tried to look at the paper and I can’t… So when they told me I could get the books [on tape], I was so enthusiastic!"

Some of her adaptive strategies have been contributed by her large and devoted family. Several months ago, A.S.’s sons found a solution to her problem with distinguishing adjacent objects such as a doors and walls, or kitchen cabinets. "I can see yellow very well, so my son put yellow tape on the doors." By taping the edges of a door, sink, or other object, A.S. is better able to distinguish object from surround, so that her house is no longer as treacherous as it once was.

At the end of our interview we asked A.S. if there was anything she would like to say to people interested in learning more about Bálint syndrome. She replied, "I’m talking to you for one reason—because I think if more people know about it, they won’t go through what I’ve gone through." A.S. describes the hope that her story might motivate physicians to seek better treatments and therapies that might allow her and other Bálint patients to take up the threads of the former lives, and to "see again."

AUTHOR CONTRIBUTIONS
Jason R. Coomes was involved in the design of the study, in data collection and analysis, and in drafting and revising the manuscript. Dr. Josef Biller was involved in the conceptualization and design of the study, in data collection and analysis, and in revising the manuscript. Dr. Murray Flaster was involved in the design of the study, in data analysis, and in revising the manuscript.

DISCLOSURE
The authors report no disclosures relevant to the manuscript. Go to Neurology.org for full disclosures.
RESIDENCY TRAINING

These manuscripts will address issues related to residency training, including educational initiatives, programs, opinions, and other topics related to neurology education and training. Relevant topics could include work hours and sleep deprivation, the role of neurocritical care or outpatient neurology in training, quality assurance initiatives, incorporation of evidence-based neurology into training, medical student teaching, work/life balance, and others. Seeking the assistance of senior faculty members is often useful.
Residency Training:
Developing a program of quality and safety
to train resident neurologists for the future

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MD
John W. Engstrom, MD

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ABSTRACT
Attention to quality and safety metrics is increasingly important for all physicians in practice due to mandates by governmental organizations, insurers, the public, and accreditation bodies. Neurology resident trainees need to acquire these skills, but little research in and outside of neurology provides guidance as to how to teach these important concepts. In the setting of new requirements mandating that training programs address these topics, we propose a number of strategies that can be implemented immediately in neurology residency training programs and call for increased investigation and sharing of best practices in order to adequately prepare neurology residents for the current and future environment of practice. Neurology® 2012;78:602-605

Quality care is defined by the Institute on Medicine as “the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge.” Many practicing physicians have traditionally viewed “quality care” as a more nebulous concept (“I know it when I see it”) that is difficult to recognize and challenging to apply to their own practice.

Measurement of quality usually involves examining structures, processes, and outcomes. Structures (e.g., having a neurologist examine any patient presenting with acute stroke) are easy to measure but are time and resource intensive to implement. Processes (e.g., prescribing an antplatelet medication on discharge for secondary stroke prevention) have been the focus of the majority of quality research and policy to date. Outcome measurement, although desirable, has been fraught with difficulties including obtaining consistent longitudinal measurements in systems with multiple tiers of health service coverage as well as patient-specific variables (e.g., medication adherence) that are beyond the control of the individual physician. Much of the quality literature has been criticized by some for concentrating on these more easily measured structures and processes as opposed to clinically meaningful outcomes, a vital issue to address in future studies.

Neurologists will be increasingly expected to demonstrate that their care is of high quality, not only by hospitals justifying the expense of physician support, but also by insurers, governmental agencies, and a public increasingly engaged in a discussion emphasizing the delivery of high-quality care.

In the late 1990s, hospitals in the United States began to track core measures thought to represent quality care. This reporting is increasingly accessible to the public, even down to physician-specific details. Neurologists certainly will be asked in the near future to measure non-neurologic aspects of patient care that hospitals are required to report. Examples include rates of appropriate deep vein thrombosis prophylaxis and hospital-acquired infections. Focusing on these non-neurologic metrics is foreign to many neurologists, and adoption and dissemination of these good practices will be an important goal for our field. Physicians are increasingly rewarded and incentivized for good quality care, through these reporting metrics and even financial incentives such as “pay for performance” packages. Ultimately, neurologists of the future will need to be attentive to neurologic quality metrics that are only beginning to be defined.

Patient safety has also become a major focus for regulatory agencies, clinicians, and the public, stemming from the now decade-old Institute of Medicine report “To Err Is Human.” National patient safety goals are transforming medicine, with hospitals reporting and tracking “never events” and so-called “preventable con-

From the Department of Neurology, University of California, San Francisco.
References e1-e9 are available on the Neurology® Web site at www.neurology.org.
Disclosure: Author disclosures are provided at the end of the article.
Presented in part at the Consortium of Neurology Program Directors’ Conference, AAN meeting, Honolulu, HI, April 2011.
ditions,” each of which carries financial and regulatory penalties. Building a “culture of safety” has become the mantra in medicine with analogies to the airline industry.

Quality and safety issues have become a major part of each practicing clinician’s daily routine and these influences are destined to expand. Despite the need to teach trainees these principles and prepare them for this new practice environment, there remains a dearth of relevant research on the topic within neurology. The Accreditation Council for Graduate Medical Education’s (ACGME) required core competencies of practice-based learning and improvement and systems-based practice hinge on trainees using quality and safety concepts to improve their own patient care and that delivered by the health care system. The ACGME milestones project will add depth to core competencies by establishing specific behaviors and accomplishments that are necessary for each trainee to reach proficiency in each competency.4

Trainees not only need to learn these skills, but they will need to be maintained, relearned, and refined throughout their career to maintain board certification. The American Board of Psychiatry and Neurology’s Maintenance of Certification Program emphasizes these concepts through performance in practice (PIP) requirements wherein physicians need to participate in quality improvement (QI) programs throughout their 10-year recertification cycle.21

Systematic reviews of teaching QI and safety reveal that only a few studies to date describe interventions that target residents.46 The results of teaching these topics to medical students and other health professions mainly have demonstrated improved knowledge regarding quality issues when a group is tested after a didactic intervention. What is lacking is proof that these interventions have meaningful clinical benefits. While some studies show improvement in a process, these benefits tend to wane over time and do not become ingrained as permanent solutions, especially in the world of residency education where thoughtful quality interventions may not be sustained when the resident “champion” graduates. This is a major challenge for resident QI projects and raises the stakes for systematic and effective involvement of residency program directors.

In the context of these challenges, we propose ideas by which neurology training programs can begin to teach quality and safety to residents within the limited confines of a training environment that is increasingly time challenged due to duty hours constraints and mandates to expose residents to an ever-widening set of clinical, administrative, and research experiences (table).

MAKE TEACHING QUALITY AND SAFETY A REQUIREMENT The ACGME common program requirements, which apply to all training programs regardless of specialty, were updated in 2011 to include language requiring programs to analyze clinical practice using QI methods and to initiate changes with the goal of improving patient care.52 Residency programs are also required to have their trainees identify systems errors and implement solutions. Participating in QI and safety programs is now a requirement for our trainees and necessary for residency and fellowship programs to maintain accreditation.

Internal medicine residents have been required by the ACGME to participate in a continuous QI process as part of their continuity clinics since 2009. This requirement has led to a number of successes and challenges that can inform neurology programs. The American Board of Internal Medicine’s Practice Improvement Modules (PIM) have been used as a tool to teach QI principles to residents.59 For example, one PIM instructs residents on evidence-based preventive medicine topics such as when to order screening colonoscopies; residents can examine their own clinical behaviors before and after this module. A similar approach in neurology could be successful in the setting of the American Academy of Neurology’s (AAN) recent publication of outpatient guidelines for quality care in various subspecialties.69

Ultimately, a successful program for teaching quality and safety will need to establish interventions that make a demonstrable difference to patient care outcomes and are sustainable over time. The University of Chicago’s internal medicine program recently focused on developing this sustainability through the use of multiple cycles of a “plan, do, study, act” structure both early and late in the training program.7

INCENTIVIZING QI GOALS In some institutions, resident incentives are used to encourage program-wide QI. At UCSF, the GME resident council sets institution-wide goals for the residents (e.g., all residents will improve their collective handwashing rate to 85%). In addition, individual residency programs propose yearly quality improvement goals (e.g., the neurology residents will increase dysphagia screening rates in stroke patients to 90%). Each proposal is vetted through a campus-wide quality group and these measures are tracked monthly with GME administrative support, giving real-time feedback to the residents as to their progress. Residents are given a financial bonus at the end of the year only if the goal is met.

These programs encourage residents to work together toward a common goal with close supervision
<table>
<thead>
<tr>
<th>Description</th>
<th>Assessment used</th>
<th>Neurology-relevant outcomes</th>
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<tbody>
<tr>
<td>TOPS project: multidisciplinary teamwork training sessions and formation of unit-based safety teams including solicitation of daily patient goals</td>
<td>Standardized surveys of patient safety culture</td>
<td>Improvement in safety culture on neuroscience-based floors with residents taking the lead as part of multidisciplinary teams</td>
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<tr>
<td>Trial of a self-directed curriculum in quality of care for internal medicine residents in an outpatient clinic including readings, weekly self-reflection with faculty members, and medical record audits</td>
<td>Self-reported behavioral changes as well as patient quality of care metrics such as improvement in hemoglobin A1c and LDL levels</td>
<td>Improvement in neurology-specific quality of care metrics such as those recently proposed in AAN outpatient quality guidelines for epilepsy and Parkinson disease</td>
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<tr>
<td>Patient safety education program with monthly conferences in a family medicine residency program focusing on ambulatory adverse medical events</td>
<td>Medical event reporting attitudes and reporting behavior before and after intervention</td>
<td>Neurology residents using a similar program could increase their reporting of untoward events and “near misses” to departmental QI and M+M committees in both outpatient and inpatient settings</td>
</tr>
<tr>
<td>Used ABIM clinical preventative services practice improvement module (PIM) to incorporate longitudinal QI curriculum and projects into required ambulatory rotations among residents</td>
<td>Multiple resident-based QI projects resulted from this PIM, each with distinct assessments; one example assessed the frequency of inaccurate medication lists in the ambulatory medical record</td>
<td>Neurology-specific projects could focus on performance in practice modules used for maintenance of certification; accurate medication lists could be targeted in a similar project given the multiple drug-drug interactions with neurologic medications such as antiepileptic drugs</td>
</tr>
<tr>
<td>Residents perform a “systems audit” for upcoming M+M conferences; upon completion of the audit, residents can critically review a case with an adverse event, identify a systems issue that led to the adverse outcome, conduct a root-cause analysis, interview stakeholders, propose solutions, and calculate costs</td>
<td>Resident awareness of systems issues, resident views of the educational value of M+M conferences, and actual institutional improvements that resulted from the systems audits</td>
<td>Neurology programs could focus on M+M cases related to tPA administration or other neurologic emergency treatments in the hospital leading to systems improvements (e.g., decreased door to tPA time)</td>
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<tr>
<td>Fellows in internal medicine subspecialties were taught root cause analysis (RCA) processes via didactic sessions and practiced conducting an RCA involving an adverse medication event</td>
<td>Faculty assessment of RCA competency as part of an objective structured clinical examination</td>
<td>Neurology residents or fellows could learn RCA skills and apply them to formal review of adverse events in outpatient and inpatient settings</td>
</tr>
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</table>

Abbreviations: AAN = American Academy of Neurology; ABIM = American Board of Internal Medicine; LDL = low-density lipoprotein; M+M = morbidity and mortality; tPA = tissue plasminogen activator; QI = quality improvement.

from program directors and local QI experts. However, one potential limitation is that some incentives chosen may be mere “low hanging fruit” selected to maximize the likelihood of success. Many goals set only address national mandates (e.g., handwashing rates) without measuring local patient outcomes that result (e.g., reduction in nosocomial infection rates). Additionally, financial incentives may only be useful to spark the initial change in behavior and may indirectly discourage sustainability; residents may no longer put effort into quality and safety processes once the financial incentive to do so has expired.

**USE MORBIDITY AND MORTALITY CONFERENCES AS A QUALITY AND SAFETY TOOL**

The morbidity and mortality (M+M) conference can serve as another method to engage residents in patient safety issues. Rather than using the conference to embarrass or “call out” mistakes, M+M conferences can be used in a blame-free manner to explore errors and “near misses” while developing systems-based methods to avoid similar future mishaps. A culture of discovery and sharing of errors is needed for these conferences to run effectively; too often senior clinicians focus conference presentations on fantastic diagnoses rather than exposing and learning from their own errors. Leadership in open disclosure and improvement goes a long way in setting the example for our young trainees.

Placing residents in leadership roles on departmental M+M committees also allows for the development of these important skills. In the medicine department at the Mayo Clinic, residents are assigned to an M+M conference in advance to perform a “systems audit,” identifying areas to both emphasize during the conference and to use in improving structures. In some programs, residents run their own M+M committee or conferences in an effort to discuss these issues in a low-stakes environment without faculty presence. These efforts make safety part of the culture of the residency program and hopefully lead to sustainable professional habits.

**FOCUS OTHER CONFERENCES ON QUALITY AND SAFETY ISSUES**

It may be also useful for residency programs to focus other traditionally didactic conferences on quality and safety issues. Presenting brief “safety vignettes,” either using local cases or those available on Web sites such as that of the Agency for Healthcare Research and Quality (AHRQ), can be a useful adjunct to conference time. Patient-centered conferences that focus on errors or “near-misses” can take the place of yet another didactic talk regarding a neurologic topic. In
some institutions, periodic “patient safety rounds,” where current inpatients are discussed with an eye exclusively on safety issues, can help address problems in real time, avoiding potential errors, and changing systems to provide safer care.

**USING ROOT CAUSE ANALYSES** Root cause analyses (RCAs) are another useful construct for trainees to learn about safety issues and develop systems-based solutions in the face of medical errors. Mandated by the Joint Commission, RCAs are advantageous because they are by nature interdisciplinary and focus on the “why” and “how” of errors rather than “who.” At the end of the process, structural changes are suggested to avoid similar mishaps in the future; these changes are usually not physician-specific, allowing trainees a window into the complex health care environment that allows for safe care within a multidisciplinary team. Ideas for success include resident-run departmental RCAs and placing residents on hospital-wide RCA committees.9

**BUILDING A CULTURE OF SAFETY** Although safety and quality metrics are often viewed as overlapping with a blurred divide, the field of safety offers a number of unique learning opportunities. The concept of building a “culture of safety” is a broad one that involves teamwork and communication among diverse providers. Many of the already mentioned interventions help to achieve this goal. Residents can play a crucial role in developing this culture and be given the opportunity to play a leadership role, interacting with nursing, pharmacy, case managers, and even patients to achieve a common goal. The TOPS project is one such published multidisciplinary, inpatient unit-based system that engages residents in developing and maintaining a culture of safety and could be used on neuroscience-focused hospital floors.10

**RESEARCH AND DISSEMINATION OF BEST PRACTICES** Given the impetus for teaching safety and quality education in neurology, residency programs need to recognize these issues as a major focus of training. Research within neurology is sorely needed and essential to the development of specialty-specific tools. Sharing best practices among programs is important as with any relatively new area of focus in education. Ultimately our trainees need to be prepared for a life in practice that continually examines QI and safety, a task in which the AAN will become an organizational hub. We must quickly develop the means to impart these skills during training or face a group of graduates ill-prepared for this aspect of the real world of neurologic practice.

**AUTHOR CONTRIBUTIONS**

Dr. Josephson was responsible for the study concept/design and drafting/revising the manuscript for content. Dr. Engstrom was responsible for drafting/revising the manuscript for content.

**DISCLOSURE**

Dr. Josephson serves as an Associate Editor of Annals of Neurology and The Neurohospitalist and as Editor-in-Chief of Journal Watch Neurology. Dr. Engstrom receives research support from the NIH.

**REFERENCES**

EDUCATION RESEARCH

As the central mission of *Neurology*, education is a top priority. This is a section for interventional educational studies, as well as more traditional educational research, such as surveys. This section will examine the way neurologists not only practice, but also the way we teach and approach education. Neurologists have traditionally been respected, perhaps above all other specialties, for their scholarship and teaching. Educational issues will therefore continue to be at the center of the mission of *Neurology*. 
Residency Training: The King-Devick test and sleep deprivation
Study in pre- and post-call neurology residents

ABSTRACT

Objective: The current study investigates the effect of sleep deprivation on the speed and accuracy of eye movements as measured by the King-Devick (K-D) test, a <1-minute test that involves rapid number naming.

Methods: In this cohort study, neurology residents and staff from the University of Pennsylvania Health System underwent baseline followed by postcall K-D testing (n = 25); those not taking call (n = 10) also completed baseline and follow-up K-D testing. Differences in the times and errors between baseline and follow-up K-D scores were compared between the 2 groups.

Results: Residents taking call had less improvement from baseline K-D times when compared to participants not taking call (p < 0.0001, Wilcoxon rank sum test). For both groups, the change in K-D time from baseline was correlated to amount of sleep obtained (r_s = −0.50, p = 0.002) and subjective evaluation of level of alertness (r_s = 0.33, p = 0.05) but had no correlation to time since last caffeine consumption (r_s = −0.13, p = 0.52). For those residents on their actual call night, the duration of sleep obtained did not correlate with change in K-D scores from baseline (r_s = 0.13, p = 0.54).

Conclusions: The K-D test is sensitive to the effects of sleep deprivation on cognitive functioning, including rapid eye movements, concentration, and language function. As with other measures of sleep deprivation, K-D performance demonstrated significant interindividual variability in vulnerability to sleep deprivation. Severe fatigue appears to reduce the degree of improvement typically observed in K-D testing. *Neurology*® 2012;78;e103-e106

GLOSSARY

K-D – King-Devick; KSS – Karolinska Sleepiness Scale.

Sleep deprivation has been demonstrated to negatively impact multiple aspects of neurocognition, including diminished attention, altered perception, impaired memory, and slowed visuomotor response.¹ Despite evidence that sleep deprivation significantly hampers neurocognitive skills, the degree of potential compensation for cognitive slowing continues to be debated. In a study of surgical residents, no abnormalities in arithmetic calculations and surgical knot tying were observed after overnight sleep deprivation.² Furthermore, substantial interindividual differences in vulnerability to sleep loss effects have been demonstrated, as a study of volunteers undergoing sleep deprivation periods ranging from 1 to 3 days showed some participants had minimal change in cognitive functioning while others had significant impairment on a battery of neurocognitive tests.³

Prior research has demonstrated that fatigue caused by sleep deprivation has a profound impact on eye movements, particularly by slowing peak saccadic velocity,⁴ increasing spontaneous blinking,⁵ and diminishing accuracy of smooth pursuit.⁶ The King-Devick (K-D) test involves rapid number naming and captures impairment of eye movements, attention, language, and other correlates of suboptimal brain function. The K-D test has recently been verified as a method to screen for

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Go to Neurology.org for full disclosures. Disclosures deemed relevant by the authors, if any, are provided at the end of this article.
concussion in athletes, with increased times associated with cognitive slowing and worse concussion outcomes.\textsuperscript{7,8}

The current research investigates the impact of sleep deprivation on eye movements and attention as measured by the K-D test in residents taking overnight call. It aims to study some unresolved questions surrounding the effects of sleep deprivation, including better identification of interindividual differences in vulnerability to sleep loss effects and quantification of the role of fatigue on K-D testing. The study hypothesizes that increased sleep deprivation will be associated with increased time and increased errors (worse performance) on the K-D test.

**METHODS** Study participants. Neurology residents and staff from the University of Pennsylvania Health System were enrolled in this study. Subjects are a convenience sample of individuals who were taking overnight call (n = 25) and individuals who were not taking call (n = 10) who were willing to undergo testing.

Standard protocol approvals, registrations, and patient consents. Study protocols were approved by the University of Pennsylvania Institutional Review Board. All participants signed written informed consent.

Participant survey. Before testing, each participant completed a survey to self-report the number of hours of sleep obtained in the prior 24 hours, approximate number of hours of sleep over the past week, timing of caffeine consumption, and evaluation of sleepiness. The Karolinska Sleepiness Scale (KSS), a commonly utilized assessment of overall tiredness based on a 9-point scale (1 = very alert, 3 = alert, 5 = neither alert nor sleepy, 7 = sleepy [but not fighting sleep], 9 = very sleepy [fighting sleep]), was used to measure the level of sleepiness in participants.\textsuperscript{9} Also, reports of the prevalence of sleep deprivation symptoms, including falling asleep during meetings and problems with memory and concentration, were obtained.

The K-D test. The K-D test is based on the time to perform rapid number naming.\textsuperscript{3} It involves reading aloud a series of single-digit numbers from left to right on 3 test cards. All participants were given the same standardized instructions prior to each testing session, specifically to read the numbers as quickly and accurately as possible. The K-D test yields scores for time (sum of number of seconds required to read each test card) and errors (total number of mistakes made on the test cards). Each participant completed 2 testing sessions, 1 as a baseline and 1 as follow-up, typically within a 24- to 72-hour time period. The first session was performed in residents and staff members when they were not postcall and after \&geq; 6 hours of sleep. In residents taking call, the second session was completed the morning after overnight call. In residents and staff members not taking overnight call, the second session was completed at the same time of day after \&geq; 6 hours of sleep. All testing was performed by a medical student blinded to the results of the first session.

**Statistical analysis.** Data analyses were performed using Stata 12.0 software (StataCorp, College Station, TX). Differences in follow-up and baseline times were compared for participants currently taking call and those not taking call using the Wilcoxon rank sum test. Associations between change in K-D test performance and duration of sleep during the call period, caffeine consumption, and subjective scoring of sleepiness were evaluated using Spearman rank correlations. For all statistical tests, type I error for significance was set at \( p < 0.05 \).

**RESULTS** Characteristics and K-D testing data for the resident and staff cohort are summarized in the table. The participants taking call did not have less sleep over the prior 24 hours at baseline \( (p = 0.82) \) but did have less sleep when postcall relative to the control group \( (p < 0.0001, \text{Wilcoxon rank sum test}) \). Less improvement from baseline K-D times were observed in residents taking call when compared to residents and staff not taking call \( (p < 0.0001, \text{Wilcoxon rank sum test}; \text{figure, A}) \). Errors on K-D testing were minimal throughout the study \( \text{(total of 7 errors)} \), but were more frequent among residents taking call both at baseline \( (1 \text{of 25 participants with at least 1 error}) \) and at follow-up \( (4 \text{of 25 with at least 1 error}) \).

Changes in K-D time scores from baseline were correlated to amount of sleep obtained for the entire cohort including subjects who were postcall and those not taking call), with less sleep associated with less improvement in K-D score \( (r_e = -0.50, p = 0.002) \). Within the postcall resident group, however, the magnitude of changes in K-D scores from baseline did not correlate with duration of sleep on call, although performance was impaired in this group. Changes in K-D time score from baseline were also modestly correlated to the subjective evaluation of sleepiness at time of testing, with greater improvement from baseline among those who reported less sleepiness \( (r_e = 0.33, p = 0.05; \text{figure, B}) \). There was no relation between changes in K-D time scores from baseline and time of last caffeine consumption \( (r_e = -0.13, p = 0.52) \) or length of sleep while on call among postcall residents \( (r_e = 0.13, p = 0.54) \).

**DISCUSSION** The K-D test is sensitive to the impact of sleep deprivation on cognitive functioning, including aspects such as rapid eye movements, concentration, and language. Participants not taking call showed a median improvement of 3.8 seconds in follow-up K-D scores, consistent with the learning effect previously described in K-D testing.\textsuperscript{7,8} However, residents had a median slowing of about 0.23 seconds on postcall K-D testing, suggesting that the learning effect was negated by sleep deprivation. While this worsening in K-D test performance is not
Table  Characteristics and scores for the neurology resident and staff cohort

<table>
<thead>
<tr>
<th>Age, y, mean ± SD</th>
<th>Residents taking call (n = 25)</th>
<th>Residents and staff not taking call (n = 10)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>30 ± 3</td>
<td>31 ± 10</td>
</tr>
<tr>
<td>Sex, n (% male)</td>
<td>9 (36)</td>
<td>5 (50)</td>
</tr>
<tr>
<td>Duration of sleep in past 24 hours at baseline, h, median (range)</td>
<td>7.5 (6.0 to 12.0)</td>
<td>7.0 (6.0 to 13.0)</td>
</tr>
<tr>
<td>Duration of sleep in past 24 hours at time of follow-up, h, median (range)*</td>
<td>2.0 (0 to 6.5)</td>
<td>6.75 (6.0 to 8.0)</td>
</tr>
<tr>
<td>KSS at baseline, median (range)*</td>
<td>3 (1 to 7)</td>
<td>4 (3 to 5)</td>
</tr>
<tr>
<td>KSS at follow-up, median (range)*</td>
<td>5 (1 to 9)</td>
<td>3 (1 to 7)</td>
</tr>
<tr>
<td>Time since caffeine intake at baseline, h, mean ± SD</td>
<td>2.2 ± 1.7</td>
<td>2.3 ± 1.9</td>
</tr>
<tr>
<td>No. of times subject has fallen asleep during a meeting/ activity, median (range)*</td>
<td>1.65 (0 to 5)</td>
<td>0.7 (0 to 5)</td>
</tr>
<tr>
<td>Baseline K-D time score, s, median (range)</td>
<td>36.9 (25.0 to 46.9)</td>
<td>38.6 (27.3 to 43.7)</td>
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<tr>
<td>Follow-up K-D time score, s, median (range)</td>
<td>37.4 (25.6 to 49.7)</td>
<td>34.9 (25.5 to 38.1)</td>
</tr>
<tr>
<td>Change in K-D time score from baseline, s, median (range)**</td>
<td>0.23 (−4.8 to 8.6)</td>
<td>−3.8 (−7.7 to −1.8)</td>
</tr>
<tr>
<td>Participants with at least 1 error on K-D testing at baseline, n (%)</td>
<td>1 (4%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Participants with at least 1 error on K-D testing at follow-up, n (%)</td>
<td>4 (16%)</td>
<td>0 (0%)</td>
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</table>

Abbreviations: K-D = King-Devick test; KSS = Karolinska Sleepiness Scale.
*Indicates a variable that was statistically significantly different between the 2 groups: p < 0.0001 for duration of sleep at time of follow-up; p = 0.02 for number of times fallen asleep; p < 0.0001 for change in K-D score from baseline.
**KSS is a subjective measure of overall tiredness with rating scale 1–9; higher scores represent greater levels of sleepiness.
***Change in K-D time score from baseline calculated as follow-up time − [baseline time]; negative numbers indicate improvement in score, consistent with mild learning effect.

as extreme as seen in a cohort of athletes with concussions (reported median 5.9-second increase in K-D time),* it demonstrates the potential effectiveness of K-D testing to detect eye movement slowing in sleep deprivation. Furthermore, postcall residents had an increased number of errors on follow-up relative to control subjects, similar to the increased number of errors observed in athletes with concussions.9 These results suggest that increased time and error on K-D testing capture the deleterious effects of sleep deprivation on eye tracking and attention.

Less sleep in the prior 24 hours was associated, in the overall cohort of on-call and noncall participants, with less improvement in K-D time from baseline. However, among residents taking call, no association was found between duration of sleep obtained on-call and K-D follow-up performance. Nonetheless, the performance on the K-D test was impaired in this group. In other words, postcall residents obtained less sleep time than subjects not taking call, which correlated to poor performance on the K-D test, but when a subanalysis of the postcall residents was completed no correlation between K-D time from baseline and sleep was observed. The finding is unlikely to be due to variability in test performance; in fact, recent studies demonstrated a high degree of test-retest reliability for K-D with intraclass correlations of 0.97.7 The result could be explained, however, by interindividual vulnerability to the effects of sleep deprivation that has been documented with other sleep deprivation measures.10 In the current study, some residents obtaining zero hours of sleep on call improved at a level similar to controls while others were significantly impaired in their K-D performance even when obtaining several hours of sleep on call. No study variable (including age, sex, time to caffeine, level of training, hospital service, or prevalence of sleep deprivation symptoms) effectively predicted which individual would be more affected by sleep deprivation. One potential confounding factor may have been the amount of caffeine consumption prior to testing; while our study captured the time since last caffeine intake, the actual quantities of caffeine were not evaluated in this study.

Self-report of increased level of sleepiness (using the KSS) was associated with less improvement in K-D times from baseline. This finding corresponds to prior research that found participants reporting an increased level of sleepiness had slower peak eye saccade velocities relative to participants rating themselves as more alert.7 Although the ability to appropriately identify level of alertness has been debated, recent evidence suggests that subjective alertness and performance are modestly correlated, with most discrepancy during the biological night.10 The association between subjective level of sleepiness and
improvement in K-D test times in the current study provides further support for the concept that individuals are fairly effective in rating their level of alertness. However, self-report of sleepiness is a subjective measure not capable of capturing individual vulnerability to sleep deprivation effects.

Severe fatigue (ratings sleepy and very sleepy on the KSS) significantly affected follow-up performance on the K-D test in the present study. Since prior research has demonstrated no effect on K-D performance from athletic workout fatigue, the current results extend our understanding of K-D testing in relation to extreme fatigue levels. In the search to objectively evaluate the effects of sleep deprivation, the K-D test offers a simple and quick method to measure degree of eye movement slowness in subjects. Further research with larger cohorts is needed to expand the subject sample size, elaborate interindividual variability in vulnerability to the effects of sleep deprivation, and evaluate the impact of different sleep loss patterns on attention and eye movements. Indeed, the K-D test offers the potential to monitor resident performance under a variety of call schedules, including night float systems, and to test the association between eye movement slowing and clinical errors.

AUTHOR CONTRIBUTIONS
E.C. Davies: collection of data, analysis and interpretation of data, drafting and revising the manuscript. S. Henderson: collection of data, revising the manuscript. Dr. Balcer: design and conceptualization of study, analysis and interpretation of data, drafting and revising the manuscript. Dr. Galetta: design and conceptualization of study, interpretation of data, revising the manuscript.

DISCLOSURE
E.C. Davies and S. Henderson report no disclosures. Dr. Balcer has received honoraria and consulting fees from Biogen Idec, Novartis, and Vaccines. Dr. Galetta has received honoraria for speaking from Biogen Idec, Novartis, and Teva. Go to Neurology.org for full disclosures.

REFERENCES
NEUROLOGY JOURNAL CLUB

*Neurology* Journal Club submissions are structured evaluations of recent *Neurology* research articles. The aim is to enhance the training of residents and fellows by instruction in the critical appraisal of medical literature. Residents or Fellows interested in submitting a *Neurology* Journal Club article should review the e-Publication Ahead of Print articles at [www.neurology.org/content/early/recent](http://www.neurology.org/content/early/recent) for the most recently published material and email *Neurology* with their selection for prior approval. Selections will aim to represent the major categories of research methodology over the course of a 3-year residency cycle. Submissions should be timely and are requested no longer than 4 weeks following the original e-Publication date of the subject article. These Journal Club critiques, written by neurology residents and fellows with faculty supervision, should follow a specific outline and contain subtitles for background and significance, hypothesis and design, methods, results, and interpretation. Rather than a critical correspondence or editorial, this feature will highlight methods for the critical appraisal of medical literature. This online feature could be used as an adjunct to traditional institutional journal clubs and promote discussion among neurologists, including trainees and those in practice.
Journal Club:
Early stroke risk and ABCD2 score performance in tissue vs time-defined TIA

In this journal club article, we evaluate a study by Giles and colleagues\(^1\) that reports stroke risk in patients with classically defined TIA subcategorized by presence or absence of radiologic brain infarction.

The concept of a TIA is evolving in parallel with better understanding of brain ischemia and insights gained from neuroimaging studies. TIAs were classically defined as a sudden focal neurologic deficit resulting from brain or retinal ischemia lasting less than 24 hours.\(^2,3\) The time threshold of 24 hours was arbitrarily chosen, and given that there is no evidence to support any single time criterion associated with infarction, this has appropriately been questioned.

A newer and well-received definition of TIA is "a transient episode of neurologic dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction."\(^4\) This definition communicates the important concept that transient symptoms can nonetheless be associated with permanent brain injury, encourages the use of neuroimaging studies, and may promote rapid interventions for acute brain ischemia.

The ABCD2 score, a risk-stratifying score for patients with TIA, is derived from the patient’s age, blood pressure, clinical features, TIA duration, and history of diabetes. This simple, validated score identifies patients at highest risk of early stroke after TIA.\(^5\) Scores are commonly divided into low risk (0–3), intermediate risk (4–5), and high risk.\(^5,6\)

The clinical ABCD2 scale is integrated in this study with results from acute brain imaging to assess how the new tissue-based definition of TIA further assists with risk stratification of patients with transient neurologic symptoms.

HYPOTHESIS AND DESIGN In this analysis of data pooled from 12 medical centers which included 4,574 patients, Giles and colleagues subcategorized TIA as “tissue positive” or “tissue negative,” depending on the presence or absence of radiographic brain infarction seen on MRI or CT scans.\(^1\) They set out to determine the added value of brain imaging to the risk stratification of patients with TIA and hypothesized that the ABCD2 score retains its prognostic value within these groups.

These questions are undoubtedly relevant to today’s clinical practice in which imaging studies are increasingly obtained and criteria for admission to the hospital are becoming stricter. Having objective, accurate means of identifying the patients at highest risk for stroke after TIA could facilitate rapid interventions and hopefully lead to better clinical outcomes.

METHODS The authors performed a systematic review of the literature in 2009 and identified 12 research centers that had sufficient prospective data of interest available. To be included, the center needed to have a cohort of patients with TIA (traditional time-based definition), ABCD2 scores, brain imaging, and clinical follow-up until at least 7 days after the TIA. Five studies were based in emergency departments, 5 in specialized neurovascular units, and 2 were population-based. ABCD2 scores were calculated by local investigators and the presence of brain infarction could be determined by a routine report from individual centers. For patients who had MRI with diffusion-weighted imaging (DWI), any acute infarct was counted as tissue-positive (whether or not the location corresponded to clinical symptoms) and for patients with CT, any infarct, regardless of age, was also considered positive. Because CT is less sensitive than MRI for the detection of acute ischemia, combining results from these different imaging modalities could potentially jeopardize the internal validity of the study results. However, this also allows the results to be generalized to a greater extent, given that CT scans are still used as the primary imaging modality for TIA evaluations at some centers.

The statistical method used to determine the predictive power of the ABCD2 score was the area under the receiver operating characteristic curve (AUC). The receiver operating characteristic curve is a graph of sensitivity against 1 – specificity\(^6\) (figure).
The closer the AUC is to 1, the better the test’s sensitivity and specificity. An AUC of 0.5, which appears as a straight diagonal line, indicates that the variable has no diagnostic capability.

Of note, the authors did not state the statistical test used for the comparison of the tissue-positive and tissue-negative groups, though based on the nonoverlapping confidence intervals and the p values reported, the comparisons are statistically significant.

**RESULTS** The authors confirmed that radiographic evidence of brain infarction in patients with TIA is a predictor of higher risk of early stroke. There was a remarkable 18-fold increase in the rate of stroke at 7 days, from 0.4% in those with negative DWI to 7% in those with positive DWI. For those with infarcts on CT scans, the 7-day risk was 3% in those with negative CT and 13% with a positive CT. The overall risk of stroke at 90 days was 2.2% in the tissue-negative group and 12% in the tissue-positive group.

However, the value of brain imaging in addition to ABCD2 score seemed to be less clear when looking at the longer-term outcome of stroke within 90 days, specifically for low-risk patients as stratified by ABCD2 score. Of patients with ABCD2 score ≤3, only 21 patients (2%) had a stroke within 90 days, but over half of these (n = 12, 57%) had tissue-negative imaging.

Nevertheless, the ABCD2 score was predictive of recurrent stroke at 7 days within both the tissue-positive and tissue-negative groups. Of 1,665 patients with ABCD2 ≤3, 10 patients (0.6%) had a recurrent stroke in 7 days, of which 7 were in the tissue-positive group. Of 2,905 patients with ABCD2 ≥4, 135 patients, or 4.6%, had recurrent stroke at 7 days. Ninety-eight of these (73%) had evidence of brain infarction on either MRI or CT.

The AUC for prediction of stroke by ABCD2 at 90 days was 0.66 for tissue-positive and 0.69 for tissue-negative patients. AUC for the prediction of stroke at 7 days was 0.68 for tissue-positive vs 0.73 for tissue-negative. Thus the ABCD2 score meaningfully stratifies risk among both the tissue-positive and tissue-negative groups.

**INTERPRETATION** In their large, international multicenter study, Giles and colleagues show that the ABCD2 score retains its prognostic value for refining the risk of stroke in both tissue-positive and tissue-negative groups. They also confirm that brain imaging adds value to the ABCD2 score by identifying patients at a higher risk within a given ABCD2 score category. Because the ABCD2 score meaningfully stratifies risk within both tissue-positive and tissue-negative groups, it indicates that the score does more than simply separate “real TIA”s from TIA mimickers. These findings add to the growing body of literature suggesting that early brain imaging (particularly DWI) enhances prediction of early stroke risk in patients with TIA.

In order to implement the author’s findings into clinical practice, routine imaging in TIA evaluation protocols would be necessary. This would best be achieved with the use of MRI, rather than CT. Based on the author’s results that patients with tissue-positive imaging after TIA had 7.5% more risk of having a stroke within the following week, one would need to image 14 (95% confidence interval 11–17.1) patients to identify one additional patient at high risk of early stroke. When extended out to assess the risk of stroke within 90 days, this number decreases to 11 (95% confidence interval 8.4–13.1).

The authors appropriately conclude that the information provided by acute imaging is clinically relevant and should influence management and triage decisions.

The results of the study are valid, though there are some inevitable limitations. The data, pooled from 12 studies, were collected over 11 years from various medical centers with assessments by clinicians with different degrees of cerebrovascular experience and using different imaging techniques. This variation in study methods threatens validity to an extent, but also reflects the reality of clinical practice more accurately. Mixing results from CT scan and MRI appears most problematic, not only because of the higher sensitivity of MRI but also because DWI can demonstrate acute lesions while this is impossible with CT scans. Still, the overall rates of stroke at 90 days were similar in this study to those found in a
prospective study that used only MRI (current study had 2.2% vs 4.3% for tissue-negative and 12% vs 10.8% for tissue-positive). Overall, these findings provide further support for the evolving concept of a tissue-based rather than the traditional time-based definition of TIA. The results make a compelling argument for the use of prompt brain imaging (specifically MRI with DWI sequences) to optimize the triage of patients with transient neurologic symptoms ascribed to focal cerebral ischemia. One specific interpretation of the data, when applying it to an emergency room situation, might be that patients with low risk ABCD2 scores (<3) with negative DWI could be discharged, while those with positive DWI should be admitted, despite the low ABCD2 score, given the substantial increased risk of stroke within the next 7 days.

Within the past few decades there have been tremendous advances in the diagnosis and treatment of cerebrovascular disorders. The results of this study support that our definitions and scoring systems should be correspondingly modified to maximize clinician decision-making with the aim of positively impacting on patient outcomes.

**AUTHOR CONTRIBUTIONS**
Dr. Fugate: drafting and revising the manuscript, interpretation of data. Dr. Rabinstein: revising the manuscript, interpretation of data, study supervision.

**DISCLOSURE**
Dr. Fugate is a member of the editorial team for the Neurology® Resident & Fellow Section. Dr. Rabinstein has a research grant from CardioNet and receives royalties for books published with Elsevier.

**REFERENCES**
MEDIA AND BOOK REVIEWS

The Neurology offices frequently receive newly published books, and residents and fellows are invited to review these. Reviewers will be allowed to keep the books. Reviews should be 250-500 words, and include the strengths and weaknesses of books for a trainee audience. Interested individuals should contact the journal (smorianity@neurology.org) for available books to review. We also welcome reviews of online, electronic, and other educational materials, and interested individuals should contact the journal to discuss their ideas.
NERVE WHIZ

Many neurology trainees have traded pocket references for smartphones, resulting in increased demand for easy-to-use and clinically relevant apps. A recent review of smartphone use in training programs found that 85% of responders own smartphones and more than half utilized apps in a medical setting.1

Nerve Whiz, designed by neuromuscular specialist Zach London, is an example of a user-friendly medical app of particular interest to neurologists. Nerve Whiz is targeted at medical professionals with an interest in the peripheral nervous system, and it serves as an anatomic review of nerve roots, plexuses, and peripheral nerves. It is free to all users and is compatible with iPhone, iPod touch, iPad, and Android devices.

Nerve Whiz is divided into 4 sections: nerve and muscle charts, a muscle localizer, nerve diagrams, and a sensory localizer. Nerve and muscle charts provide the user with a comprehensive database of muscles that can be sorted anatomically—for example, by root, trunk, or cord—or by action. The muscle localizer allows the user to select the muscles of interest, and it then provides relevant localizations. This feature links to the diagram section, which can also be accessed independently. Here, the user can review nerve and muscle diagrams of the brachial or lumbar-sacral plexuses. The final section of the interface, the sensory localizer, allows the user to touch a region of interest; Nerve Whiz then shows relevant reflexes, the muscles supplied by that nerve, and a visual representation of the nerve’s sensory distribution.

The app’s strength lies in its dual role as a teaching and diagnostic tool. On the way to a consult, residents can review relevant anatomy and potential localizations in the nerve and muscle charts. After performing an examination, they can input which muscles were strong or weak into the muscle localizer, and Nerve Whiz aids in localization and the development of a thoughtful differential diagnosis. In the common scenario that multiple localizations are possible, Nerve Whiz reminds the user which additional muscle groups or nerve distributions to test for clarification.

There are a few areas, however, in which Nerve Whiz could improve. While the user interface of Nerve Whiz is largely straightforward, the diagram section is cumbersome to navigate on a smaller device. The muscle localizer and muscle charts would benefit from supporting pictures of relevant muscle groups. As advertised on its Web site, Nerve Whiz is not intended to be used in isolation to make clinical decisions and is no substitute for a thorough understanding of peripheral nervous system anatomy.

Nonetheless, Nerve Whiz is the first resource of its kind, and medical professionals of all levels of training will find that the app provides clinically relevant content through an intuitive interface. Nerve Whiz is an indispensable addition to any trainee’s toolkit.

Reviewed by Monica Lemmon, MD

The author reports no disclosures. Go to Neurology.org for full disclosures.

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REFERENCE

NEURO TOOLKIT
created by Kent Ellington, MD, http://neurotoolkit.blogspot.com, $2.99

At the start of my neurology residency, I strove for organization and efficiency in my evaluation of patients in the emergency ward. Unfortunately, I often found myself frantically searching through a disorganized stash of sheets and handouts for protocols on treating status epilepticus, calculating a stroke scale, or testing visual acuity. I yearned for an efficient method to rapidly access neurologic reference information. The Neuro Toolkit app for the iPhone and iPad provides such a solution at a competitive price for residents and fellows ($2.99). Unlike bulkier applications that take several seconds to load and update, Neuro Toolkit launches instantaneously to an opening screen with 8 self-explanatory icons that neatly organize a set of medical calculators (e.g., corrected phenytoin levels, ABCD2 TIA scale), clinical scoring scales (e.g., Unified Parkinson’s Disease Rating Scale, Expanded Disability Status Scale), and other reference information (e.g., McDonald criteria, American Academy of Neurology brain death criteria, antiepileptic drug dosing). My personal favorites are the Snellen Eye Chart and NIH Stroke Scale, the latter of which allows quick access to the standardized images and phrases to screen for dysarthria, aphasia, or visual neglect. The creator of Neuro Toolkit, Kent Ellington, regularly updates the application based on user feedback. The current version could be improved by adding a dermatome map, Ishihara plates, and the spinal and nerve innervations of common muscle groups. I recommend Neuro Toolkit to all neurology practitioners as an up-to-date, simple, and straightforward app that will assist in the evaluation of patients in a wide range of settings, from the emergency room to the outpatient clinic.

Reviewed by Vaishnav Krishnan, MD, PhD

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Teaching NeuroImages: 
Differential diagnosis of scapular winging

Figure 1
Right scapular winging caused by weakness of ipsilateral trapezius [A–C: arrow depicts the upper trapezius atrophy; D: arrow depicts the atrophy in upper trapezius and asterisk depicts the normal infraspinatus on coronal T1-weighted right shoulder MRI], rhomboids [E–G: arrow and asterisk depict atrophy of infraspinatus and rhomboids, respectively], and serratus anterior [H: arrow depicts the contracting lower trapezius causing medial displacement of scapula]

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Supplemental data at www.neurology.org

Scapular winging (SW) is caused by weakness of trapezius, rhomboids, and serratus anterior muscles. The different patterns of scapular movement among these causes assist in the differential diagnosis and are illustrated in the 3 described cases (table e-1 on the Neurology® Web site at www.neurology.org).1,2

Case 1 (figure 1, A–C) presented with right SW (lateral displacement of superior angle that became evident at arm abduction) due to upper trapezius weakness and atrophy that is also evident on shoulder MRI (figure 1D and figure e-1). Case 2 (figure 1, E–G) had right SW (lateral displacement of inferior angle that was accentuated when the patient pushed his elbow backwards against resistance) due to rhomboids weakness. Case 3 (figure 1H) had right SW (medial displacement of scapula that was enhanced during forward arm flexion) due to serratus anterior weakness.

AUTHOR CONTRIBUTIONS
Dr. Tsivgoulis: study design, drafting and revising the manuscript. Dr. Vadikolias: data collection, critical comments during manuscript revision. Dr. Courcoutsakis: data collection, critical comments during manuscript revision. Dr. Heliopoulos: data collection, critical comments during manuscript revision. Dr. Stamboulis: drafting and revising the manuscript. Dr. Piperidou: drafting and revising the manuscript.

REFERENCES

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E-Pearl of the Week: Bright Tongue Sign

October 2, 2012

Bright Tongue Sign

In patients with amyotrophic lateral sclerosis (ALS), brain magnetic resonance imaging (MRI) may show pronounced hyperintensity of the tongue on T1–weighted sequences, giving the appearance of a “bright tongue”. This appearance is caused by fatty replacement of the tongue muscle, which has been chronically denervated due to the effects of motor neuron disease. Other abnormalities of the tongue in ALS on MRI include may include a reduced tongue size, as measured in the sagittal plane, a more square or rectangular shape, and a change in tongue position so that it no longer contacts the hard or soft palate.

Reference

Submitted by:
Jennifer E. Fugate, DO

Disclosure:
Dr. Fugate serves on the editorial team for the Neurology® Resident and Fellow Section.
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