2020 ANNUAL HIGHLIGHTS OF THE RESIDENT & FELLOW SECTION
HOW CAN I CONTRIBUTE?

The Neurology® Resident & Fellow (R&F) Section provides countless opportunities for trainees to make an introductory contribution to the field. We have over 12 categories of manuscripts, from Global and Community Health to Clinical Reasoning cases. Every year, the R&F team develops innovative submission opportunities and new ways to engage our readers and users.

EXPLORE THE R&F SITE
Access NPub.org/RF for the latest blogs, articles, e-Pearls, Mystery Cases, and other trainee resources. The print issue also features “Resident & Fellow Rounds”—a monthly summary of the R&F Section articles.

SUBMIT AN E-PEARL
These brief educational points often tie in to a Neurology article, podcast, or item on the website. Each should consist of 85 words or less and one reference.

BECOME A PEER REVIEWER
Create an account at submit.neurology.org and include any expertise terms that interest you. After your profile is complete, contact the editorial office at rfsection@neurology.org and you will be added to the database of available reviewers.

FOLLOW NEUROLOGY ON SOCIAL MEDIA
Receive the R&F Section alerts including e-Pearls, Mystery Cases, and recently published article alerts.

ANSWER OUR MYSTERY CASE QUESTIONS
Disseminated via our social media sites, emails, and our website, these mini-cases pose fascinating questions for the reader and provide instructions for submitting your answers.

CHECK OUT A TOPIC
The R&F team members have compiled a list of prospective topics for authors under the following subcategories: Child Neurology, Opinion & Special Articles, and Emerging Subspecialties.

ACCESS THE AUTHOR GUIDES
The R&F Author Center provides pictorial guides on writing Clinical Reasoning, Pearls & Oy-sters, and Teaching NeuroImages at NPub.org/rfsections.

HAVE MORE QUESTIONS? HAVE AN IDEA?
Contact the editorial office at rfsection@neurology.org
MRI: Contrast-enhancing lesion in the cavernous sinus with perifocal edema and contact to the chiasm and the blood vessels. 68Ga-DOTATATE PET/CT: high 68Ga-DOTATATE uptake. Hematoxylin & eosin staining: noncaseating epithelioid granulomas. CD68 staining: tightly packed epithelioid macrophages. Gomori staining: incipient perigranulomatous fibrosis surrounded by leukocyte common antigen (LCA)–positive lymphocytes (magnification ×20, bars 100 μm).
Dr. Roy Strowd, assistant professor of neurology and oncology, is a neurologist and neuro-oncologist at the Wake Forest Baptist Medical Center. He graduated magna cum laude from Duke University in 2005 and from the Wake Forest School of Medicine in 2009. He completed residency in neurology at Wake Forest Baptist Medical Center in 2013 where he served as chief resident. He pursued fellowship training at Johns Hopkins completing the clinical and research Neuro-oncology Fellowship Program as well as dedicated training in medical education research through a fellowship supported by the American Academy of Neurology’s Medical Education Research Training Fellowship. Strowd has clinical research interests in drug development and response assessment in neuro-oncology as well as medical education interests in exploring optimal approaches for teaching healthcare professionals at multiple levels of training. Strowd is active in medical education, academic scholarship, and scientific research at both the local and national levels and truly enjoys each opportunity to mentor residents and fellows throughout neurology.

Rachel Gottlieb-Smith, MD

Rachel Gottlieb-Smith is a child neurologist at the University of Michigan. She graduated from Harvard College with a concentration in psychology. She received her MD from the Johns Hopkins University School of Medicine, and completed her residency in child neurology at the Children’s Hospital of Philadelphia. She is a recipient of the American Academy of Neurology’s Medical Education Research Training Fellowship for the 2018-2019 academic year and is pursuing additional training in medical education through the Master of Health Professions Education program at the University of Michigan.

Katherine Fu, MD

Katherine Fu is an adult neurology resident at the University of California, Los Angeles. She graduated with degrees in neuroscience and biological sciences from the University of Southern California and obtained her medical degree from the Keck School of Medicine of the University of Southern California. Her research interests include investigating neuroimaging biomarkers of neurodegenerative diseases. She also has an interest in medical education, having served as a neuroanatomy teaching assistant and neurology clerkship instructor in medical school.

Malik Muhammad Adil, MD

Malik Adil is a neurology resident at Ochsner Clinic Foundation, New Orleans. He received his bachelor’s degree in medical technology from Jinnah Post Graduate Medical Center and medical degree from Shifa College of Medicine, Pakistan. Prior to neurology residency, he served as a clinical research fellow at Zeenat Guresh Stroke Center, University of Minnesota, where he engaged in research on stroke. In addition to stroke, he is interested in amyloid angiopathy, cerebral microbleeds, vascular dementia, neurological biomarkers, and developing simple educational tools for teaching neurology to medical students, residents and fellows. He is currently a vascular neurology fellow at NIH.

Guilermo Delgado-Garcia, MD

Guilermo Delgado-Garcia is a senior neurology resident and MSc student at the Instituto Nacional de Neurología y Neurocirugía in Mexico City. He received his medical degree from the Universidad Autónoma de Nuevo León (UANL), Mexico. After graduating medical school, he spent one year at the Instituto Nacional de Ciencias Médicas y Nutrición, Mexico, as a research assistant. He then completed residency in internal medicine at the University Hospital of the UANL. This year, he will start a clinical fellowship in epilepsy and EEG at the University of Calgary in Canada.

Kwo Wei David Ho, MD, PhD

Kwo Wei David Ho is a pain medicine fellow at Stanford University. He graduated from the University of Virginia with degrees in Chemistry and Physics. He then went on to obtain his MD and PhD through the Medical Scientist Training Program (MSTP) at the University of Iowa. His PhD was in genetics, with focus on the genetics of seasonal depression and bipolar disorder. He then completed his neurology residency training at the University of Florida. His current research interests include pain genetics and neuromodulation for chronic pain. Outside of medicine, Ho enjoys kayaking, cycling, and rock climbing.
Robert Hurford, MSc, MRCP (UK)
Robert Hurford is a neurology resident at Cambridge University Hospital, UK. He graduated in medicine from the University of Nottingham in 2011 followed by a master’s in clinical neuroscience at the Institute of Neurology, UCL. He has since pursued joint academic and clinical training, working with several stroke research groups, including in Manchester, Cambridge, and Paris. He is currently completing a DPhil (PhD) at the University of Oxford, funded by an Association of British Neurologists’ Clinical Research Training Fellowship. His research interests include clinical imaging, health economics and epidemiology of cerebrovascular disease. Outside work he enjoys long-distance running and learning languages.

Regan Jo Lemley, MD, MS
Regan Lemley is a chief adult neurology resident at Wake Forest School of Medicine. She graduated from Southwestern University with a BS in biology and minor in philosophy, and she obtained a master’s degree in medical sciences prior to attending medical school at Texas Tech SOM. She is passionate about neurology education and curriculum development, and her research interests include exploring the influences of psychosocial factors and hormonal changes on epilepsy. She will be an epilepsy fellow at Brigham and Women’s Hospital after completion of residency. Her hobbies include distance running, hiking, and embroidery.

Ariel Maia Lyons-Warren, MD, PhD
Ariel Lyons-Warren is an instructor in child neurology at Texas Children’s Hospital and Baylor College of Medicine in Houston Texas. She earned her Bachelor of Arts from Johns Hopkins University with a major in neuroscience and a minor in writing seminars. She then completed the medical scientist training program at Washington University in St. Louis. Her PhD research focused on the role of inhibition in temporal coding and she continues to be interested in how inhibition shapes neural circuits. After medical school, she matched into the basic neuroscience research track in the child neurology residency program at Texas Children’s. Her clinical interests include medical education, palliative care, and sensory processing disorders.

Jodie Roberts, MD, MSc
Jodie Roberts is an adult neurology resident at the University of Calgary in Canada. She earned her Master of Science in epidemiology while completing her medical degree at the University of Calgary. She has broad research interests within the field of neuroepidemiology, with emphasis on health outcomes. Outside of medicine, she enjoys cycling, cross-country skiing, and hiking in the beautiful Rocky Mountains.

Aaron Rothstein, MD
Aaron Rothstein is a fellow in neurovascular disease at the University of Pennsylvania. He completed his neurology residency at the New York University School of Medicine. He writes regularly about medicine for The New Atlantis at http://practicing-medicine.thenewatlantis.com/. In his spare time, Aaron enjoys swing dancing, running, and cycling.

Jeffrey Russ, MD, PhD
Dr. Jeff Russ is a child neurology fellow at the University of California San Francisco (UCSF). He graduated in 2008 with a Bachelor of Arts in the biological basis of behavior from the University of Pennsylvania. He then entered the Weill Cornell/Sloan Kettering/Rockefeller University Tri-Institutional MD-PhD Program, where he earned a PhD in neuroscience in the laboratory of Dr. Julia Kaltschmidt. He studied how interneuron development is affected by intrinsic transcription factor expression and extrinsic circuit perturbations, such as perinatal stroke. Russ graduated with his MD and PhD in 2016. He then completed pediatrics training at UCSF.

Behnam Sabayan, MD, PhD
Behnam Sabayan is an adult neurology resident at Northwestern Memorial Hospital, Northwestern University, Chicago. He will start his fellowship in vascular neurology at Massachusetts General Hospital, Harvard University. Sabayan has an established interest in brain aging and in particular the vascular contribution to brain structural and functional integrity. After medical school he received a Master of Science (MSc) in aging and vitality and his PhD in clinical neuroscience from Leiden University in the Netherlands. He has been a close collaborator with neuro-epidemiology and population science lab at NIA/NIH and has published more than 60 peer-reviewed papers.

Jens Witsch
Jens Witsch is an adult neurology resident at Yale University. He is originally from Freiburg/Germany and studied medicine at the University of Heidelberg. Before graduating from medical school, he engaged in a one-year research thesis in electrophysiology at the Max Planck Institute for Medical Research in Heidelberg investigating in vivo neuronal physiology in an epilepsy mouse model. He then completed neurology residency at the Charité in Berlin under the mentorship of Matthias Endres, Christoph Flöner, and Eric Jüttler, followed by a neurocritical care research fellowship.

Ariel Lyons-Warren, MD, PhD
Ariel Lyons-Warren is an instructor in child neurology at Texas Children’s Hospital and Baylor College of Medicine in Houston Texas. She earned her Bachelor of Arts from Johns Hopkins University with a major in neuroscience and a minor in writing seminars. She then completed the medical scientist training program at Washington University in St. Louis. Her PhD research focused on the role of inhibition in temporal coding and she continues to be interested in how inhibition shapes neural circuits. After medical school, she matched into the basic neuroscience research track in the child neurology residency program at Texas Children’s. Her clinical interests include medical education, palliative care, and sensory processing disorders.

Fábio Nascimento, MD
Fábio Nascimento is a neurology resident at Baylor College of Medicine. Originally from Brazil, he completed medical school at the Universidade Federal do Paraná (UFPR) and then spent two years at the University of Toronto working as a research fellow in epilepsy genetics. Subsequently, he moved to Houston, TX, to train as an adult neurologist. After residency, he will pursue a two-year clinical neurophysiology and epilepsy fellowship at Massachusetts General Hospital and then begin his career as an academic epileptologist. Outside of neurology, Nascimento enjoys listening and dancing to sertânejo (a typical Brazilian music genre), going to the movies, eating lots of sushí, and working out.

Alonso G. Zea Vera, MD
Alonso G. Zea Vera is a child neurology resident at Cincinnati Children’s Hospital Medical Center. He received his medical degree from the Universidad Peruana Cayetano Heredia, Peru. His research interests include neurophysiology, movement disorders, and cognitive neuroscience. Outside medicine he enjoys playing soccer and spending time with his dog.
Announcement

Neurology Resident & Fellow Section Writing Award

The Winner of the 2020 Award Is:

Bryan J. Neth, MD, PhD

Right brain: Art and the restoration of identity in dementia

See page 60 of this Highlights book.

The Neurology Resident & 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 & 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 a resident or fellow in one of the neurologic 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 2021 and will be awarded for a paper published in 2020.

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

PAST RECIPIENTS

2019 Award Winner
Emerging Subspecialties in Neurology: Pain medicine
Nathaniel M. Schuster, MD, and Jacob R. Hascalovici, MD, PhD

2018 Award Winner
Clinical Reasoning: An 82-year-old man with worsening gait
Sheena Chew, MD; Ivana Vodopivec, MD, PhD; and Aaron L. Berkowitz, MD, PhD
Neurology November 21, 2018, 89:21e246-e252

2017 Award Winner
Pearls & Oysters: Episodic ataxia type 2: Case report and review of the literature
Elan L. Guterman, MD; Brian Yurgionas, MD, MS; and Alexandra B. Nelson, MD, PhD
Neurology June 7, 2016, 86:23 e239-e241

2016 Award Winner
Emerging Subspecialties in Neurology: Telestroke and teleneurology
Sunil A. Mutgi, MD; Alicia M. Zha, MD; and Reza Behrouz, DO
Neurology June 2, 2015, 84:22 e191-e193

2015 Award Winner
Clinical Reasoning: An unusual cause of transverse myelitis?
Pavan Bhargava, MD, and Rodger J. Elble, MD, PhD
Neurology February 11, 2014, 82: e46-e50

2014 Award Winner
Right Brain: A reading specialist with alexia without agraphia: Teacher interrupted
Jason Cuomo, MA; Murray Flaster, MD, PhD; and José Biller, MD
Neurology January 7, 2014, 82:e5-e7

2013 Award Winner
Clinical Reasoning: A 55-year-old woman with vertigo: A dizzying conundrum
Daniel R. Gold, DO, and Stephen G. Reich, MD
Neurology October 23, 2012, 79:e146-e152

2012 Award Winner
Child Neurology: Brachial plexus birth injury: What every neurologist needs to know
Christina B. Pham, MD; Johannes R. Kratz, MD; Angie C. Jelin, MD; and Amy Gelfand, MD
Neurology August 16, 2011, 77:695-697

2011 Award Winner
Right Brain: We were all once ‘fixed and dilated’
Amy Gelfand, MD
Neurology November 16, 2010, 75: 1851
QuIC Thinking: The Role of RT-QuIC in the diagnosis of Sporadic Creutzfeldt-Jakob Disease

Sporadic Creutzfeldt-Jakob Disease (sCJD) is a rare, uniformly fatal prion disease. Diagnosis requires a supportive clinical history, examination, MRI, EEG and, previously, nonspecific CSF findings including elevations in tau and protein 14-3-3. The real time quaking induced conversion (RT-QuIC) test is a CSF assay specific for the detection of the abnormal prion protein (PrP) with a sensitivity and specificity of 92% and 100%, respectively. Recent changes to the CDC sCJD diagnostic criteria reflect its utility requiring only a neuropsychiatric syndrome and a positive CSF RT-QuIC for the diagnosis of probable sCJD. The RT-QuIC represents an opportunity to identify and confirm atypical cases of sCJD.

References

Submitted by Colin Casault, MD, neurologist and current general critical care fellow—University of Calgary, Alberta, Canada. Dr. Casault was accepted for a two-year Neurocritical Care Fellowship at Partner’s HealthCare in Boston, Massachusetts.

Dr. Casault reports no disclosures.

Cogan's Rule

Cogan's Rule

Named after David G. Cogan, who described a series of 31 anatomically verified cases in 1959, this rule states that, in a patient complaining of homonymous hemianopia, if there is an asymmetric optokinetic response (lack or diminished response in the direction of the corrective saccade when the optokinetic nystagmus (OKN) stimulus moves towards the affected lobe), the lesion is more likely to involve the deep portions of the parietal lobe that are outside the territory of the posterior cerebral artery and therefore the lesion is unlikely of vascular origin. In contrast, the asymmetric optokinetic response is usually associated with tumors, as tumors are more common in the parietal than the occipital lobe.

References

Submitted by: Roberto Rodríguez, MD, Neurology Resident at the National Institute of Neurology and Neurosurgery (México City, México)

Dr. Rodríguez-Rivas reports no disclosures.
Neurology® Resident & Fellow Section

John J. Millichap MD, Roy E. Strowd III, MD

The mission of the Neurology Resident & Fellow Section (RFS) is to keep our readers up to date on issues related to training and career considerations as well as support the development of lifelong learning skills. The RFS was launched in 2004 by Robert “Berch” Griggs, then the editor-in-chief of Neurology, and Karen Johnston, associate editor. Currently, the RFS is trainee-run by an editorial team of more than 20 neurology residents and fellows with the responsibility for reviewing, editing, and publishing articles. Residents are selected annually through a competitive process that attracts dozens of applicants, and each will serve a three-year term. This past year, the eligibility was changed to include trainees from anywhere in the world. Past editorial team members have gone on to other important editorial activities, at Neurology and elsewhere, and they have found the experience a formative part of their careers. Dr. John Millichap, a former editorial team member and the current RFS Section Editor, assumed leadership of the section from Dr. Elkind in 2015. He is joined by Deputy Section Editor Roy Strowd, another former editorial team member. Photographs and brief biographies of the current Resident & Fellow Section editorial team can be found in this Highlights booklet.

The number of submissions to the RFS has increased dramatically (from 12 in 2004 to 738 in 2019), and the quality of published manuscripts has improved. The RFS publishes primarily case reports and opinion pieces, with scientific research articles limited to education research. The subsections are curated by the RFS Editorial Team members and focus on (1) case-based clinical neurologic education, including Clinical Reasoning, Pearls & Oy-sters, Child Neurology, Teaching NeuroImages, and Mystery Cases; (2) graduate medical education, including Journal Club, Global and Community Health, and Education Research; and (3) career issues, including Emerging Subspecialties in Neurology. Descriptions of these subsections appear in this Highlights booklet and include the top representative articles published in the past year as selected by the RFS Editorial Team members.

In addition to writing and reviewing for the journal, the RFS Editorial Team members have initiated and developed multiple unique projects over the years, including podcasts (beginning in 2007), weekly E-Pearls (2008), an annual Writing Award (first given in 2009), and our website (launched in 2010). Our ongoing 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 2012. In 2012, we also began making all Teaching NeuroImages available as teaching slides. In 2014, members of the RFS editorial team were awarded the American Academy of Neurology Education Research Grant to study the role of mentored peer review of journal articles as a way of teaching evidence-based medicine and peer review skills to residents. The research project involved residents at nine US residency programs, and the results were presented at the AAN and other national meetings. In 2015, Luca Bartolini, editorial team member of the RFS, developed his original idea for “Practice Current: An interactive exchange on controversial topics” in collaboration with the editors of Neurology® Clinical Practice. This has become a wildly popular section of NCP that aims to identify and discuss difficult clinical scenarios and diseases with conflicting or insufficient evidence regarding diagnosis or treatment. Other notable successful initiatives include two books, Clinical Reasoning and Child Neurology, of previously published cases compiled to provide an educational resource for trainees and program directors. One of the greatest accomplishments of the RFS is the mentor-mentee program designed to pair new RFS team members with recent graduates of the section. This program expanded to serve as a structured model for bringing new, young peer reviewers into the process, even outside the RFS itself.

The RFS webpage has exciting features such as the blog, special e-Pearls formatting, listings of the latest RFS articles, and online survey platform for the Mystery Cases. There are also links to other resident and fellow resources on the Neurology website and at AAN.com. We publish one RFS article in every print issue of Neurology, and there is a “Resident and Fellow Rounds” commentary written monthly by the RFS section editors that provides summaries of the RFS articles published with each issue. The RFS editorial team members are proud of the additional exposure through print distribution and expect that this will undoubtedly encourage the continued submission of high-quality manuscripts. Recognizing the role of social media in medicine and daily life, the RFS delivers regular Instagram posts and is involved in the Neurology Minute™ podcast as well.

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. Accordingly, the RFS is strongly supported by Neurology’s current Editor-in-Chief Robert A. Gross, Executive Editor Patty Baskin, editorial staff, the AAN, and the publisher Wolters Kluwer. In particular, staff members Kathy Pieper and Robert Withrow have provided continual assistance and encouragement without which the section could not have survived. We welcome submission of manuscripts for the Resident & Fellow Section, and author instructions can be found at 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 online 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 John Millichap, Roy Strowd, or Kathy Pieper at rfssection@neurology.org. We hope you enjoy this year’s edition of the Highlights of the RFS!

John J. Millichap, MD, FAAN, Section Editor, Resident & Fellow Section

Roy E. Strowd, MD, Deputy Section Editor, Resident & Fellow Section
Top 10 Ways for Program Directors to Use the Resident & Fellow Section

By Ariel M. Lyons-Warren, Guillermo Delgado-Garcia, Kathleen Pieper, Roy Strowd, and John J. Millichap

10. Choose a Clinical Reasoning case to systematically work through a patient presentation with residents during morning report, noon conference, in small groups, or an education conference. Published cases are chosen for their significant teaching value or originality and provide an opportunity to reinforce clinical reasoning skills as you go through presentation, diagnostic investigation, and treatment in a question-answer format.

9. Include e-Pearls at the end of email announcements to your residents and fellows to add a quick “gem” of learning. e-Pearls provide a focused insight into a Neurology related topic in 85 words or less and often highlight less commonly known features of a disease. Visit the e-Pearls archive at blogs.Neurology.org/epearls/. Now it’s fully searchable!

8. Read the Education Research subsection to get ideas for new initiatives to try in your program. This subsection reports high-quality research on educational topics and often features novel tools and interventions residents have used to improve education. You can also share these articles as a helpful resource for rising chief residents who are exploring new approaches to resident education or encourage residents to submit the results of an education-based QI project.

7. Use Teaching NeuroImages PowerPoint slides for bedside instruction. Teaching NeuroImages and Video NeuroImages are brief case reports with an associated image or video. These graphics feature classic presentations of uncommon disorders or rare presentations of common conditions and are readily available in PowerPoint format. They make for great teaching!

6. Pick sample cases from the new Child Neurology book which features clinical cases portraying different types of child neurology presentations and includes chapter introductions that compare the adult and pediatric perspective. This is an invaluable resource for both pediatric and adult neurology programs. The book can be freely downloaded in PDF format at npub.org/cnbook.

5. Try to solve the Mystery Case along with your residents and give a small prize to trainees who get all the answers right. This subsection features a case with an undisclosed diagnosis and provides the opportunity to test your knowledge of relevant pathology in a multiple-choice format. Respondents can track their performance over time and compare their answers with others online. Explanations and performance statistics are published in the following issue of Neurology. This case is also featured on our Facebook page (@AANResidentsAndFellows).

4. Look through our R&F Section blog to stay up to date on all the exciting initiatives available to residents and fellows through the AAN. Through these posts we announce new initiatives for the R&F Section as well as upcoming events of special interest to trainees. For instance, opportunities to participate in new subsections or RFS-related talks and events at the Annual Meeting. Our blog is part of Neurology Blogs and can be found here: blogs.Neurology.org/rf/.

3. Check out the newly designed Training in Neurology subsection at Neurology.org/cfa/opinion_special_articles to learn about all issues related to educating the next generation of neurologists. This subsection covers all aspects of training and pipeline development in neurology for secondary school, undergraduates, medical students, residents, fellows, pre- and post-docs.

2. Circulate copies of our new visual author guides among residents or fellows who are interested in submitting manuscripts. These pictorial guides serve as a tip sheet to help avoid common mistakes for our three most popular subsections and are an invaluable tool for anyone submitting to the RFS. You can also encourage trainees who are interested in publication to sign up to be a reviewer for the Section, or even apply for a spot on the editorial team. Our author guides are available here: Neurology.org/rf/author_guides.

1. Follow the RFS on Social Media using the hashtag #NeurologyRF on Twitter and Instagram to make sure you never miss the latest publications in the Section. Our new Instagram posts (@aanbrain) are cell phone compatible, so you can consult our content anywhere at any time. Last but not least, don't forget to share our content on Facebook, Twitter, and Instagram, so more trainees around the world can discover it!
Life after the Resident & Fellow Section: Alumni Survey Results

With 28 of over 65 former Resident & Fellow Section (RFS) member responding, RFS alumni report a significant impact of the RFS editorial board participation on their career trajectory. After graduating from the section, the majority of editorial board members go onto academic practice (92%) while the minority pursue non-academic hospital-based (4%) or private practice clinic (4%). Alumni reported many benefits of the RFS editorial board including: learning to critically appraise the neurological literature, understanding the “inner workings” of a journal and editorial process, and collaboration with other neurology trainees from around the world.

Participation in the RFS was a gateway to continued participation in scholarly peer review. After rotating off the RFS editorial board, 63% of RFS alumni went on to review for Neurology the main journal, 42% for Neurology® Clinical Practice, and 96% continued to review for the Neurology RFS. Most also participate as peer reviewers in other journals including New England Journal of Medicine, Journal of Graduate Medical Education, JAMA Neurology, Epilepsia, Journal of Neuro-Oncology, Pediatrics, Stroke, PLoS One, and over 30 other journals!

Alumni found their participation in the RFS editorial board to also be a springboard to other academic or scholarly opportunities in neurology. Several now serve in editorial capacities with Neurology as well as with other journals including as associate editor for the Journal of Graduate Medical Education, Clinical and Investigative Medicine, Brain & Life®, or others. One alumnus commented that “The RFS was my first formal engagement with the AAN beyond SIGN and the Annual Meeting. It was a great introduction to a great society. Now I serve on multiple committees and advise the leadership development program.” Another reported that being an RFS editorial board member had “huge impact! It helped me understand the ins and outs of academic publishing early!”

Advice for current neurology trainees from RFS editorial board alumni

“The RFS provides inspiring mentorship and guidance so that you can become an effective reviewer. You do not need to have extensive reviewing experience to apply. Get engaged early and often!”

“We have a long tradition of teaching our specialty using illustrative cases from our clinical practice. Going forward, our patients and their stories will still provide invaluable opportunities to learn our craft and where we should be heading as a specialty.”

“Always keep an eye for interesting cases to write a case report or case series. Ask your mentors to suggest papers to write. These projects are doable during residency.”

“An interesting case or topic will always get due consideration from the Resident and Fellow section.”

Figure 1:
What is the biggest impact of having served on the Neurology Resident & Fellow Section for your career?
Disputes & Debates: Rapid online correspondence

The editors encourage comments on recent articles through Disputes & Debates:

Access an article at Neurology.org/N and click on “COMMENT” beneath the article header.

Responses will be posted within three business days.

Before submitting a comment to Disputes & Debates, remember the following:

- Disputes & Debates is restricted to comments about studies published in Neurology within the last eight weeks
- Read previously posted comments; redundant comments will not be posted
- Your submission must be 200 words or less and have a maximum of five references; reference one must be the article on which you are commenting
- You can include a maximum of five authors (including yourself)

Visit the Neurology Resident & Fellow Website

Click on the Resident & Fellow Section menu dropdown at Neurology.org or visit NPub.org/rf directly.

Now offering:

- Blogs of interest to trainees and educators
- Neurology Resident & Fellow Editorial team information
- “Search by Subcategory” option
- E-pearl of the Week
- Mystery Case surveys
- RSS Feed
- Direct links to AAN resources
- Recently published Resident & Fellow articles
Child Neurology

The Child Neurology section in the Resident & 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: Spastic paraparesis and dystonia with a novel ADCYS5 mutation

Marissa Dean, MD, Ludwine Messiha, PhD, Gregory M. Cooper, PhD, Michelle D. Amaral, PhD, Salman Rashid, MD, Bruce R. Korf, MD, PhD, and David G. Standaert, MD, PhD.


We describe a 21-year-old woman with lower extremity spasticity, dystonia, and weakness. She was born full term without complications. At 5 years of age, she began dragging her right foot, which slowly progressed to bilateral toe walking and a wide-based stance. By 14 years of age, she walked with her legs in a fixed posture with knees extended, and by 21 years of age, she was unable to stand unassisted. Family reported an intermittent hand action tremor and large “jerks” of her legs in the evening. They also noticed intermittent slurred speech that was difficult to understand. She reported occasional tingling in her fingers and toes. She completed the 5th grade, but schooling was eventually stopped because of learning difficulties. There is no family history of similar problems or consanguinity. Neurologic examination showed scanning and slurred speech, decreased strength and spasticity in the lower extremities, and a mild, low-amplitude, high-frequency terminal action tremor of both hands. Reflexes were increased at the knees (grade 3) with upgoing plantar responses, and there was decreased vibration and proprioception sensation at the toes. Upon standing, she had dystonic posturing of bilateral lower extremities.

MRI of the brain showed diffuse T2 and T2 fluid-attenuated inversion recovery hyperintensities in the white matter that were most prominent in the left frontal lobe (figure, A), right cerebellum, left caudate, and left lateral putamen (figure, B). There was also mild cerebellar vermis atrophy (figure, C), and magnetic resonance spectroscopy showed a low N-acetylaspartate peak (figure, D). An extensive workup, including metabolic and heavy metal screening, CSF analysis, EMG, nerve conduction studies, and muscle biopsy, was unremarkable. A hereditary spastic paraplegia (HSP) panel with next-generation sequencing was unrevealing. A 6-week trial of high-dose carbidopa/levodopa did not improve symptoms, and baclofen caused significant sedation.

Whole genome sequencing (WGS) revealed a likely pathogenic heterozygous missense mutation in exon 1 (M1 domain) of the ADCYS5 gene (c.697T>C, p.Tyr233His). Previously reported pathogenic ADCYS5 mutations have been associated with dyskinesias, including dystonia, chorea, and diurnal exacerbations of movement disorders.1–5 More recently, a phenotype resembling spastic paraparesis was reported in association with an ADCYS5 mutation.6 In this article, we discuss the approach to patients with multiple abnormal movements, along with a brief overview of the ADCYS5 mutation phenotype.

Initial evaluation and diagnostic approach for multiple abnormal movements

When a patient presents with multiple abnormal movements, the most important first step is to correctly define the phenomenology. This includes recognition of hyperkinetic movements such as chorea, dystonia, and tremor, as well as hypokinetic movements such as bradykinesia and akinesia. Once the movements are defined, the clinician should identify the most prominent abnormal movement, as this will guide the differential diagnosis and workup. The age at onset, progression of symptoms, and accompanying clinical features may add additional clues to the diagnosis. A detailed family history, including presence of consanguinity, should be
obtained to aid in identifying a mode of inheritance: autosomal dominant, autosomal recessive, X-linked recessive, or sporadic. Based on the phenomenology, most prominent abnormal movement, clinical and family histories, and accompanying examination features, a proper differential diagnosis can be created and a workup initiated. It is, however, important to realize that these steps are merely a guide. If an initial workup is unrevealing for the dominant abnormal movement, one should consider a workup based on the accompanying abnormal movements.

In our case, both spastic paraparesis and dystonia were prominent abnormal neurologic findings. Spastic paraparesis is formally defined as lower limb spasticity and weakness. While spastic paraparesis is not usually considered a movement disorder, it can lead to abnormal gait patterns and abnormal movements. Dystonia refers to “sustained or intermittent muscle contractions causing abnormal, often repetitive, movements, postures, or both.” When dystonia and spastic paraparesis coexist, identifying the dominant clinical symptom, along with the age at onset, can help guide the workup. For example, if childhood-onset

spastic paraparesis is the most prominent symptom, an initial workup should include MRI of the brain and spinal cord in order to identify structural lesions or white matter abnormalities. In contrast, if childhood-onset dystonia is the most prominent symptom, the initial workup should include MRI of the brain as well as CT imaging of the head to evaluate for basal ganglia calcifications. In addition, screening for potentially treatable diseases (table) is highly advisable for patients with spastic paraparesis or dystonia.

**Differential diagnosis for childhood-onset spastic paraparesis and dystonia**

The differential diagnosis for childhood-onset spastic paraparesis and dystonia includes several conditions (table). If present, additional clinical features may assist in narrowing the differential diagnosis further. In our patient, we considered metabolic disorders such as Krabbe disease, metachromatic leukodystrophy, cerebral folate deficiency, cerebrotendinous xanthomatosis (CTX), biotinidase deficiency, and primary


<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Additional clinical features</th>
<th>Diagnostic test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wilson disease</td>
<td>Kayser-Fleischer rings, behavioral changes</td>
<td>Serum ceruloplasmin, 24-hour urinary copper excretion</td>
</tr>
<tr>
<td>Glucose transporter 1 deficiency</td>
<td>Seizures, developmental delay</td>
<td>CSF glucose, SLC2A1 gene testing</td>
</tr>
<tr>
<td>Primary monoamine neurotransmitter disorders</td>
<td>Diurnal variation of symptoms</td>
<td>Levodopa trial</td>
</tr>
<tr>
<td>GTP-CH1 deficiency</td>
<td>Development delay, hypotonia, oculogyic crises</td>
<td>CSF neurotransmitters</td>
</tr>
<tr>
<td>AADC deficiency</td>
<td>Development delay, microphaly, ataxia</td>
<td>MRI of the brain and spine</td>
</tr>
<tr>
<td>Demyelinating disease (such as multiple sclerosis)</td>
<td>Fluctuating neurologic, ocular, or psychiatric symptoms</td>
<td>CT head</td>
</tr>
<tr>
<td>Fahr disease</td>
<td>Other organ system involvement</td>
<td>EMG, nerve conduction studies, or muscle biopsy</td>
</tr>
<tr>
<td>Mitochondrial disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CTX*</td>
<td>Cataracts, early atherosclerosis</td>
<td>Serum cholesterol, CYP27A1 gene testing</td>
</tr>
<tr>
<td>Vitamin E deficiency</td>
<td>Ataxia, neuropathy</td>
<td>Serum vitamin E level</td>
</tr>
<tr>
<td>Vitamin B12 deficiency</td>
<td>Neurupathy, myelopathy</td>
<td>MRI of the spine, serum vitamin B12 and methylnicotinic acid levels</td>
</tr>
<tr>
<td>Biotinidase deficiency</td>
<td>Hearing loss, cutaneous signs</td>
<td>Urine organic acids, plasma acylcarnitine, serum biotinidase level</td>
</tr>
<tr>
<td>Hereditary spastic paraparesis</td>
<td>Urinary or GI symptoms, other neurologic symptoms (cognitive problems, epilepsy) in complex HSPs</td>
<td>HSP gene panel, WGS</td>
</tr>
<tr>
<td>Leukodystrophies</td>
<td>Epilepsy, neuropsychiatric symptoms, developmental delay</td>
<td>Enzymatic testing</td>
</tr>
<tr>
<td>Krabbe disease (galactocerebroside (\beta)-galactosidase deficiency)</td>
<td></td>
<td>Galactocerebroside (\beta)-galactosidase</td>
</tr>
<tr>
<td>Tay-Sachs disease (hexosaminidase A deficiency)</td>
<td></td>
<td>Hexosaminidase A</td>
</tr>
<tr>
<td>Metachromatic leukodystrophy (arylsulfatase A deficiency)</td>
<td></td>
<td>Arylsulfatase A</td>
</tr>
<tr>
<td>Torsion dystonias</td>
<td>Tremor</td>
<td>Dystonia gene panel, WGS</td>
</tr>
<tr>
<td>ADCYS-related dyskinesias</td>
<td>Axial hypotonia, developmental delay, other hyperkinetic movements</td>
<td>WGS</td>
</tr>
</tbody>
</table>

Abbreviations: AADC = aromatic \(l\)-amino acid decarboxylase; CTX = cerebrotendinous xanthomatosus; GI = gastrointestinal; GTP-CH1 = guanosine triphosphate cycohydrase 1; HSP = hereditary spastic paraplegia; WGS = whole genome sequencing.

* Potentially treatable disorders.

It is important to recognize that primary monoamine neurotransmitter disorders (commonly referred to as dopa-responsive dystonias) improve with treatment of levodopa, and that these disorders may also present with a phenotype that resembles spastic paraparesis. Finally, Wilson disease should be considered as many phenotypes, including those with multiple abnormal movements, have been described in association with this treatable disease.

**Genetic testing for spastic paraparesis and dystonia**

There are many options available for genetic testing, including testing for single genes, gene panels, whole exome sequencing, and WGS. If spastic paraparesis is a prominent finding on examination, then genetic testing with an HSP panel is an appropriate first step. Likewise, if dystonia is believed to be a more prominent finding, then a dystonia panel may be considered first for genetic testing. If no pathogenic variants are identified through panel testing, then we recommend considering WGS since it is now readily available for clinical use. In our patient, the first genetic test that was ordered was an HSP panel, which did not reveal any pathogenic variants. We then proceeded to WGS, which revealed a novel variant in the ADCYS gene. This variant was determined to be likely pathogenic based on several criteria. The variant had not been reported in large population databases (1000 Genomes or the ExAC databases), thus indicating it is not a common variant.
In addition, this variant was predicted to cause dysfunction to the ADCYS gene through in silico analysis (damaging by SIFT, probably damaging by PolyPhen, and a CADD score of 22.2). Parental studies, including maternal and paternal identity testing, indicated the variant arose de novo, meaning the variant was not present in either parent. Previously reported pathologic variants within the ADCYS gene produced dyskinesias, chorea, or dystonia in affected patients.\textsuperscript{1,5} For these combined reasons, the variant was predicted to be likely pathogenic by the American College of Medical Genetics and Genomics guidelines (PS2, PM2, PP3, PP4).\textsuperscript{11}

**ADCYS gene mutations and clinical phenotypes**

The ADCYS gene encodes adenylyl cyclase 5, which converts adenosine triphosphate into cyclic adenosine monophosphate.\textsuperscript{12} Pathogenic ADCYS variants are usually expressed in an autosomal dominant pattern, although an autosomal recessive inheritance pattern has recently been described.\textsuperscript{1,3} It is important to recognize that when there is no family history of a similar phenotype, it is possible that a pathogenic mutation may arise de novo as well.

Neurologic symptoms associated with an ADCYS gene mutation were first described in a German family, which was originally classified as autosomal dominant familial dyskinesia with facial myokymia.\textsuperscript{7} Subsequently, additional individuals with ADCYS genetic variants have been described. These individuals most frequently exhibit hyperkinetic movements, especially chorea.\textsuperscript{3,4} Other common clinical features include axial hypotonia, facial chorea/dystonia, diurnal exacerbations of movement disorders, minimal to no cognitive impairment, and little to no progression of symptoms.\textsuperscript{4} Of these common features, our patient only exhibited diurnal exacerbations of movement disorders that were described as large jerks of her legs at night. She had less common features of developmental delay/cognitive impairment and progression of her symptoms. For a review of ADCYS phenotypes, see "Phenotypic insights into ADCYS-associated disease."\textsuperscript{9} Interestingly, a recent case report describes a woman with a phenotype more closely resembling our patient: spastic paraparesis, dystonia, hyperreflexia, and progression of symptoms.\textsuperscript{11} This patient had a missense mutation within the M2 domain of the ADCYS gene, while our patient’s mutation lies within the M1 domain. Sensory symptoms have not been well-described in ADCYS gene mutation patients. However, since no other cause was identified in our patient, we postulate that her sensory symptoms may be related to her gene mutation.

Brain MRI abnormalities were not reported in the initial cases of ADCYS gene mutations and are not typically associated with the disorder. However, one patient with an ADCYS pathogenic variant exhibited hypointensities within the globus pallidus interna bilaterally, but this pattern was different from that seen in our patient.\textsuperscript{4} In addition, the recently reported case with a spastic paraparesis phenotype did not have abnormalities on brain MRI.\textsuperscript{6} Because the finding in our patient of white matter involvement on brain MRI is not a common feature of ADCYS mutations, we evaluated for other causes of leukoencephalopathy. However, none was found, and thus we suspect this finding may be attributable to the ADCYS variant.

**Treatment options for ADCYS-related dyskinesias**

There is currently no specific treatment for ADCYS-related dyskinesias. Medications are selected based on the specific abnormal movement but have resulted in limited success in ADCYS-associated dyskinesias.\textsuperscript{13} Preventative treatment should be utilized through a multidisciplinary approach with physical therapy and occupational therapy to prevent future complications from immobility and spasticity.

When evaluating a child with multiple abnormal movements, accurate identification of the phenomenology guides further workup and management. For a patient presenting with childhood-onset spastic paraparesis and dystonia, MRI should be included in the initial workup. In addition, treatable conditions need to be considered for these patients, which includes dopa-responsive dystonia, CTX, vitamin E deficiency, Wilson disease, and biotin deficiency, among others (table). When an etiology is not revealed, WGS may be a helpful tool to identify rare disorders. With this additional case of a spastic paraparesis and dystonia phenotype associated with an ADCYS gene mutation, we propose the addition of ADCYS to spastic paraparesis gene panels.

**Author contributions**

M. Dean: drafting and revising the manuscript, study concept and design. L. Messiaen: revising the manuscript, analysis and interpretation of data. G.M. Cooper: revising the manuscript, analysis and interpretation of data. M.D. Amaral: revising the manuscript, analysis and interpretation of data. S. Rashid: revising the manuscript and study concept. B.R. Korff: revising the manuscript, analysis and interpretation of data. D.G. Standaert: revising the manuscript, analysis and interpretation of data.

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**Disclosure**

The authors report no disclosures relevant to the manuscript. Go to Neurology.org/N for full disclosures.
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Clinical Reasoning

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. See published samples as examples.
Clinical Reasoning: A misdiagnosis of atypical trigeminal neuralgia

Jaclyn R. Duvall, MD, and Carrie E. Robertson, MD


Section 1

A 47-year-old man presented with right-sided facial pain that started 2 years prior. He described the pain as extremely intense, stabbing along the right jaw, lasting 5–60 seconds. This pain was exacerbated by chewing, and to a lesser degree, by brushing his teeth. The pain was so intense that he avoided eating when possible, leading to a 20 pound weight loss. When he did eat, he would try to chew on the left side of his mouth. Around the onset of these symptoms, he also noticed a persistent numbness and burning extending from the right lower earlobe to the lateral angle of the jaw that was exacerbated by turning his head to the right.

The patient was given a diagnosis of atypical trigeminal neuralgia (TN) and sent to our headache clinic for further management.

Questions for consideration:
1. What features are typical and atypical for classical TN?
2. What is your differential diagnosis in this patient presenting with facial pain?
Section 2

TN is characterized by "recurrent paroxysms of unilateral pain in the distribution(s) of one or more divisions of the trigeminal nerve," most often the maxillary and mandibular divisions. As outlined by the International Classification of Headache Disorders, 3rd edition, TN pain:

A. Does not radiate beyond the trigeminal distribution
B. Lasts from a fraction of a second to 2 minutes (recurrent paroxysms may occur in clusters lasting longer)
C. Is severe in intensity and electric shock-like, shooting, stabbing, or sharp in quality
D. Is precipitated by innocuous stimuli within the trigeminal nerve distribution

Patients tend to be asymptomatic between paroxysms, though a subset of patients may develop a prolonged continual background pain, with fluctuations in intensity and periods of remission and recurrence that parallel the paroxysmal pain. Approximately 99% of patients with TN report at least some of their attacks being associated with a trigger. In one large study, the most commonly described triggers were gentle touching of the face (83% of patients) and talking (59%), followed by chewing (41%) and tooth brushing (36%). When cutaneous triggers are present, the most common trigger zones are around the mouth and nose, though anywhere on the face may be described. Some patients may notice a transient refractory period following a paroxysmal pain, where additional pain cannot be triggered. In contrast to the classic paroxysmal, shooting, stabbing, or shock-like qualities used to describe neuralgic pain, neuropathic pain tends to involve more persistent burning, tingling, or numbness. If the patient has features of neuropathy (numbness), persistent pain, bilateral pain, isolated supraorbital involvement, or a lack of sensory triggers, an alternative diagnosis should be considered. This could include dental pathology, parotid pathology, or an alternative neuralgia/neuropathy. See the table for a comprehensive overview of conditions that may mimic TN.

Our patient described paroxysmal severe shooting facial pain, lasting seconds at a time. He reported innocuous triggers, including chewing and possibly brushing his teeth. Interestingly, however, he denied all other classical TN triggers, including cutaneous triggers. He also described an atypical persistent pain that was more neuropathic (numbness/burning) than neuralgic, and this extended over the angle of the jaw and into the pinna of the ear, both territories that are outside of the distribution of the trigeminal nerve. Given the atypical presentation, we were concerned about an alternative diagnosis.

Questions for consideration:
1. What additional historical details should be asked to narrow the differential?
2. What additional examination tests might be helpful?
<table>
<thead>
<tr>
<th>Condition</th>
<th>Most common location</th>
<th>Pain characteristics</th>
<th>Aggravating factors</th>
<th>Things you should know or look for</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dental</td>
<td></td>
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</tr>
<tr>
<td>Caries</td>
<td>Affected tooth</td>
<td>Intermittent to continuous dull</td>
<td>Sweet foods, hot or cold stimuli</td>
<td>Visible decay</td>
</tr>
<tr>
<td>Cracked tooth</td>
<td>Affected tooth</td>
<td>Intermittent dull or sharp</td>
<td>Biting/chewing, hot or cold stimuli</td>
<td>Often difficult to visualize crack</td>
</tr>
<tr>
<td>Dry socket</td>
<td>Affected tooth</td>
<td>Continuous, deep, sharp</td>
<td>Hot or cold stimuli</td>
<td>Loss of clot, exposed bone</td>
</tr>
<tr>
<td>TMJ dysfunction (TMJ disease)</td>
<td>Jaw and surrounding muscles, radiation to ear and temple</td>
<td>Constant or intermittent, tender, aching</td>
<td>Forced mouth opening, jaw manipulation, chewing</td>
<td>May be complication of arthritis, jaw locking or popping</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>Nasal passages, above the eyes, cheeks</td>
<td>Pressure, tenderness, aching</td>
<td>Bending over</td>
<td>Fever, swelling, purulent nasal discharge, reduced sense of smell and taste, positive CT or endoscopy</td>
</tr>
<tr>
<td>Parotid</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Sialadenitis</td>
<td>Submandibular or parotid region</td>
<td>Gradual, constant</td>
<td>Tender to palpation</td>
<td>Swelling, erythema over the gland, fever, chills</td>
</tr>
<tr>
<td>Salivary stone</td>
<td>Submandibular or parotid region</td>
<td>Intermittent, dull</td>
<td>Salvation (eating or smelling foods)</td>
<td>Tenderness at gland, palpable stone, lack of salivary flow</td>
</tr>
<tr>
<td>FBS</td>
<td>Submandibular or parotid region</td>
<td>Paroxysmal, severe, sharp</td>
<td>Salvation (eating or smelling foods)</td>
<td>No sensory triggers, history of prior head/neck surgery, improves after a few bites</td>
</tr>
<tr>
<td>Neoplasm</td>
<td></td>
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</tr>
<tr>
<td>Benign/malignant</td>
<td>Submandibular or parotid region</td>
<td>Persistent dull pain</td>
<td>Swallowing, opening mouth widely</td>
<td>Lump or swelling, facial numbness, muscle weakness if masseter involved</td>
</tr>
<tr>
<td>Giant cell arteritis</td>
<td>Temporal region or holoccephalic</td>
<td>Typically continuous dull pain (new or worsening)</td>
<td>Scalp or vessel tenderness</td>
<td>Visual disturbance, jaw claudication, fevers/chills, night sweats, weight loss, TESR/CRP, temporal artery biopsy</td>
</tr>
<tr>
<td>Carotid</td>
<td></td>
<td></td>
<td>Head/neck movement</td>
<td>Evaluation for Horner for all carotid pathology (ptosis/miosis/anhidrosis)</td>
</tr>
<tr>
<td>Dissection</td>
<td>Neck, lower face/jaw, retro-orbital</td>
<td>Thunderclap or acute tearing pain or progressive or throbbing</td>
<td>Head/neck movement</td>
<td>May have preceding trauma to neck or whiplash injury</td>
</tr>
<tr>
<td>Carotidynia</td>
<td>Tender carotid bifurcation, may radiate to ipsilateral face or ear</td>
<td>Variable temporal patterns, aching/tenderness, sore throat</td>
<td>Pressure over carotid artery, coughing, swallowing, Valsalva, cold weather, head movement</td>
<td>Controversial—imaging may reveal focal eccentric thickening of the carotid wall leading to luminal narrowing, but is otherwise normal</td>
</tr>
<tr>
<td>Primary headache disorders</td>
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<tr>
<td>Migraine</td>
<td>Hemisensory ≈ holoccephalic</td>
<td>Pulsating or throbbing, lasting 4 hours or more</td>
<td>Physical activity, lights, sounds, certain foods, hormonal changes</td>
<td>Nausea, sensory phobias (light/sound), stereotypical attacks, family history</td>
</tr>
<tr>
<td>SUNCT</td>
<td>Orbital, supraorbital, or temporal</td>
<td>Severe, stabbing, lasting a few seconds to a couple of minutes</td>
<td>Usually spontaneous; can have sensory triggers include touching face/scalp, chewing, talking, coughing, blowing nose, light</td>
<td>Astrocitic features (conjunctional injection, tearing, rhinorrhea, facial flushing/sweating, ptosis/miosis)</td>
</tr>
<tr>
<td>Neuropathies</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Allodynia and hyperalgesia commonly seen with all neuropathies</td>
</tr>
</tbody>
</table>

Continued
<table>
<thead>
<tr>
<th>Condition</th>
<th>Most common location</th>
<th>Pain characteristics</th>
<th>Aggravating factors</th>
<th>Things you should know or look for</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNO</td>
<td>Unilateral distribution of trigeminal nerve, V2/V3 most common</td>
<td>Numbness, burning, continuous, paresthesia or dyesthesias</td>
<td>Light touch</td>
<td>Further diagnostic evaluation indicated especially if progressive as this may be the first manifestation of tumor or relapse of prior neoplastic process. Trauma is most common mechanism leading to TNO (often iatrogenic).</td>
</tr>
<tr>
<td>Idiopathic</td>
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<tr>
<td>Neoplastic</td>
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<tr>
<td>Inflammatory/autoimmune</td>
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<tr>
<td>Traumatic</td>
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<tr>
<td>Blunt, dental</td>
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<tr>
<td>Anesthesia dolorosa</td>
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<tr>
<td>Numb chin syndrome (&quot;mental neuropathy&quot;)</td>
<td>Unilateral lower lip and chin</td>
<td>Numbness</td>
<td>Light touch, biting lip</td>
<td>Red flag association with breast, lung, and lymphoproliferative malignancies, although dental procedures are most common culprit.</td>
</tr>
<tr>
<td>Postherpetic neuralgia</td>
<td>Dermatome of single nerve or nerve root</td>
<td>Continuous or intermittent, electrical, burning, sharp</td>
<td>Light touch in affected dermatome</td>
<td>Vesicles or scarring from herpetic rash; despite its name, postherpetic neuralgia is actually a neuropathy or neurapraxia.</td>
</tr>
<tr>
<td>Burning mouth syndrome</td>
<td>Mouth, gums, lips</td>
<td>Burning, continuous</td>
<td>No clear factors</td>
<td>May be seen with xerostomia, candidiasis, GERD, poor oral hygiene.</td>
</tr>
<tr>
<td>Other neuralgias</td>
<td></td>
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</tr>
<tr>
<td>Glossopharyngeal neuralgia (CN IX)</td>
<td>Ear, base of tongue, tonsillar fossa, angle of the jaw</td>
<td>Paroxysmal severe, electrical, shooting, stabbing, sharp</td>
<td>Swallowing, yawning, coughing, touching the ear</td>
<td>10% of cases associated with syncope/arrhythmia, consider Holter monitor.</td>
</tr>
<tr>
<td>Nervus intermedius neuralgia (&quot;geniculate neuralgia&quot;) (CN VII)</td>
<td>Deep inside and behind ear &gt; face/jaw</td>
<td>Paroxysmal severe, electrical, stabbing, sharp</td>
<td>Touch over or within the ear canal (cotton swabs)</td>
<td>May occur with Bell palsy; disorders of lacrimation, salivation, and taste may occur.</td>
</tr>
<tr>
<td>Cervical cutaneous neuralgias</td>
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<tr>
<td>Great auricular neuralgia (branch of C2 and C3)</td>
<td>Anterior (preauricular, parotid, jaw angle); posterior (mastoid and posterior/inferior pinna)</td>
<td>Paroxysmal severe, electrical, shooting, stabbing, sharp</td>
<td>Turning head/neck position during sleep, exertion, lifting ipsilateral arm</td>
<td>Neuralgia of the great auricular and lesser occipital nerves differ from neuropathy (no numbness); look for mass or irritation near nerve course.</td>
</tr>
<tr>
<td>Lesser occipital neuralgia (branch of C2 and C3)</td>
<td>Posterior scalp, superior pinna, supra-auricular scalp</td>
<td>Paroxysmal severe, electrical, shooting, stabbing, sharp</td>
<td>Movement, tenderness over posterior skull base</td>
<td></td>
</tr>
</tbody>
</table>
Section 3

A careful history is essential in the diagnosis of lower facial pain and should include the following:

- Head/neck surgery or trauma
- Cancer and systemic symptoms (fever/chills, night sweats, weight loss)
- Dental disease/procedures
- Symptoms suggestive of sympathetic pathway injury (ptosis or miosis)
- Clicking or popping of the jaw
- Rash (vesicles)
- All aggravating/relieving factors: swallowing, yawning, chewing, movement of temporomandibular joint, light touch, cool breeze or cold, head/neck positions, straining, talking, brushing teeth

On further questioning, our patient recalled a surgery just prior to the onset of pain, involving resection of a parapharyngeal pleomorphic adenoma for which he underwent resection via a right cervico-parotid approach. Follow-up MRI and magnetic resonance angiography revealed no tumor recurrence or other pathology to explain his neuropathic symptoms. On an extensive review of his triggers, he explained that while chewing on the right side did consistently trigger severe pain, if he could "push through," the pain would subside after a minute, raising the question of a TN refractory period. Most interestingly, however, he also revealed that just thinking about food or smelling food could trigger similar severe pain. With regard to the constant burning pain over the angle of the jaw and ear, this was milder and did not fluctuate with his paroxysmal pains.

On examination, our patient had reduced pin sensation over the right lower ear extending along the angle of the jaw. Given the unusual triggering of pain with food smells, we performed a bedside provocation of salivation by giving the patient a sour candy. Even before putting the candy in his mouth, the patient began to experience his typical paroxysmal stabbing pain. This became severe when he put the candy in his mouth, prior to any chewing. After chewing for about 5 seconds, the excruciating pain settled back down to his constant numbness and burning. The remainder of his neurologic examination was normal.

Questions for consideration:
1. What is the likely diagnosis for this patient’s stabbing pain?
2. What additional diagnosis might he have?
Sympathetic secretomotor innervation of the parotid produces a small amount of thick saliva that inhibits secretion, whereas parasympathetic secretomotor input produces a large volume of watery saliva that stimulates secretion. Loss of sympathetic innervation to the parotid gland leads to denervation of sympathetic receptors located on parotid myoepithelial cells, which also contain parasympathetic receptors. These receptors are hypothesized to become hypersensitive to parasympathetic stimulation, resulting in a very intense contraction of these myoepithelial cells at the first bite.

Our patient’s case was complicated by a concurrent diagnosis of great auricular neuropathy presenting as constant numbness and burning along the lower earlobe to the lateral angle of the jaw. The great auricular nerve is a peripheral branch of the superficial cervical plexus that wraps around the sternocleidomastoid, before dividing into 2 branches that provide sensory innervation to the lower ear and the angle of the jaw, often extending the length of the mandible to the lateral chin (figure). Its superficial location makes it vulnerable to traumatic andiatrogenic injury, especially following rhytidectomy (facelift), carotid endarterectomy, and other cervical surgeries.

Discussion

Our case demonstrates a classic presentation of FBS initially misdiagnosed as atypical TN. Facial pain isolated to the V3 distribution can pose a diagnostic challenge for even the most experienced neurologist. While well-recognized among head

Figure Sympathetic and parasympathetic innervation of the parotid gland

The sympathetics are supplied by the sympathetic chain coming off of the superior cervical ganglion. The parasympathetic innervation comes off of a branch of the auriculotemporal nerve. The inset on the right shows the great auricular nerve wrapping around the sternocleidomastoid to provide sensory innervation over the lower ear and angle of the jaw. Our patient, like many patients undergoing surgery to the deep parotid region, had injury to both the sympathetics as well as great auricular nerve resulting in first bite syndrome with concurrent lower face numbness. Image used with permission of Mayo Foundation for Medical Education and Research. All rights reserved.
and neck surgeons as a potential surgical complication, FBS is not often considered by neurologists during the evaluation of lower facial pain. Similar to our patient, these surgeries can also be complicated by cutaneous neuropathies (especially great auricular or auriculotemporal nerves) or iatrogenic Horner syndrome, highlighting the potential diagnostic challenge in these cases.

Although the pain of FBS may resolve spontaneously, associated pain with this syndrome can be significantly disabling, leading to avoidance of food completely and in some cases, significant weight loss and malnutrition. No consensus exists for the best treatment strategy. Early parotidectomy in the context of malignant parotid tumors has consistently relieved pain. Anticonvulsants, alone or in combination with tricyclic antidepressants, may decrease the severity or duration of the pain. Recently, botulinum toxin injections into the parotid gland have been employed with success, although a standard method of injection is not established and the duration of pain relief is variable.

FBS, although rare, should be considered in the differential of V3 distribution facial pain and its heightened awareness may enhance the neurologist’s ability to accurately diagnose this condition.

Acknowledgment
The authors thank Margaret A. McKinney for her work and artistic contribution for the illustration.

Study funding
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Disclosure
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Appendix: Authors

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<tr>
<th>Name</th>
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<tr>
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<td>Author</td>
<td>Drafting and revision for intellectual content</td>
</tr>
</tbody>
</table>

References
Call for Voices: Lived Experiences

The editors of the Neurology specialty site Equity, Diversity, & Inclusion encourage you to submit short first-person accounts (1,000 words or less) of experiences lived within the realm of equity, diversity, and inclusion (EDI) with the goal of informing and enlightening our community on these critical issues. Some topics to consider include, but are not limited to:

- Descriptions of personal experiences that shaped your views of EDI.
- Reflections on the intersection between personal identity and career.
- Discussions at the intersection of EDI and neurology patient care, research, education, advocacy, or policy.

Submit your contributions to journal@neurology.org and include “Voices Submission” in the subject line.

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Access an article at Neurology.org/N and click on “COMMENT” beneath the article header.

Responses will be posted within three business days.

Before submitting a comment to Disputes & Debates, remember the following:

- Disputes & Debates is restricted to comments about studies published in Neurology within the last eight weeks
- Read previously posted comments; redundant comments will not be posted
- Your submission must be 200 words or less and have a maximum of five references; reference one must be the article on which you are commenting
- You can include a maximum of five authors (including yourself)
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.
Education Research: An experiential outpatient teleneurology curriculum for residents

Mitra Afshari, MD, MPH, Natalie P. Wilcox, MD, and Nicholas B. Galifianakis, MD, MPH

Abstract

Objective
Telemicine is rapidly becoming a major vehicle of delivering neurologic care to patients who have limited access to subspecialists and exaggerated travel hardship. However, neurology residents receive little to no training in telemicine in outpatient clinics.

Methods
We piloted, to our knowledge, the first formalized, experiential outpatient teleneurology curriculum. Neurology residents in their third and fourth postgraduate years (PGY3 and PGY4) at the University of California San Francisco completed an interactive lecture and 4 weeks of teleneurology clinics at the San Francisco Veterans Affairs Medical Center. Change in residents' telemicine knowledge and perspectives on the utility, challenges, benefits, and future practice implementation of teleneurology were evaluated in 11 residents using precurriculum and postcurriculum quizzes and surveys after 2 of 4 weeks on the rotation.

Results
Residents' performance on quizzes improved from 53% to 88% ($p = 0.002$). Residents' impression of video visits compared to in-person visits changed, with more individuals indicating video visits to be the same if not somewhat superior with regards to obtaining a focused history, formulating a focused assessment and plan, communicating recommendations, and the overall care provided ($p \leq 0.04$). All residents felt more competent using telemicine for patient care in their eventual career.

Conclusion
Our formal didactic and clinic-based teleneurology curriculum for neurology residents, which shared core themes suggested by the 2017 American Academy of Neurology Telemedicine Work Group's published recommendations, showed a statistically significant improvement in knowledge and perspectives about the promise and limitations of teleneurology practice, as well as increased comfort levels in future implementation.
Glossary

AAN = American Academy of Neurology; SFVAMC = San Francisco Veterans Affairs Medical Center; UCSF = University of California San Francisco.

In recent years, telemedicine technology has evolved rapidly, becoming more user-friendly and inexpensive, to the point that it is becoming standard of care in many health care settings. Since telemedicine increases access to care and patient convenience, satisfaction for patients, caregivers, and providers is understandably high.\textsuperscript{[2-5]} Given the aging population, anticipated shortage of neurologists, treatable emergencies like stroke, chronic but treatable neurologic conditions like Parkinson disease, and increased travel burden due to cognitive impairment and immobility, outpatient neurologic care is poised to greatly benefit from expanded use of telemedicine. Therefore, 21st-century neurologists must be able to effectively use telemedicine in their clinical careers. However, to date, resident experience in teleneurology in outpatient clinics is scant. Recognizing this gap, the American Academy of Neurology (AAN) Telemedicine Work Group published the first model framework for a teleneurology curriculum for neurology residents in 2017.\textsuperscript{[4,5]}

In the year prior to this publication, the authors had launched a novel, formalized experiential outpatient teleneurology curriculum for University of California San Francisco (UCSF) neurology residents, implemented at the San Francisco Veterans Affairs Medical Center (SFVAMC). The current study evaluates this curriculum's effect on resident knowledge about telemedicine, their perspectives on the challenges and benefits of teleneurology practice, and their self-assessed competence in teleneurology practice.

Methods

Study population

The study involved 12 neurology residents at UCSF who completed their teleneurology rotation across their PGY3 and PGY4 years and consented to anonymously participate in precurriculum and postcurriculum assessments. Of these 12, 11 residents completed both assessments, but one resident did not complete a postcurriculum assessment and thus was excluded from the analysis. The study was approved by the UCSF institutional review board and participants were consented in writing with a brief script describing the study, anonymity, and means to withdraw participation at the start of each assessment.

Intervention

In July 2016, we launched the teleneurology rotation, in which all current PGY3 and PGY4 neurology residents rotated through 2 nonconsecutive 2-week blocks built into their yearly schedule (figure). Given that the Department of Veterans Affairs has been a leader in implementing telemedicine as part of standard care, the foundation for a hands-on, clinic-based teleneurology rotation at the SFVAMC was already in place. Residents participated in SFVAMC outpatient clinics in general neurology, movement disorders, neuromuscular, and epilepsy, seeing new or follow-up patients through live video-conferencing clinic-to-clinic or clinic-to-home visits using Cisco Jabber software. Residents also performed e-consultations with attending physician oversight, that is, asynchronous provider-to-provider consultative communications within a shared electronic medical record that do not necessitate a clinical visit.

The first few video visits were led by attending physicians experienced in telemedicine. Residents thereby gained familiarity with the technology, aspects of a history and neurologic examination unique to telemedicine, and interacting with family members and third-party staff over video. Subsequently, residents conducted their own video visits and discussed their preliminary evaluation privately with the attending. Both the resident and attending physician would then rejoin the patient to provide a final assessment, re-live the relevant components of the teleneurologic examination, and convey the plan.

Following a year of experience with the clinical rotation, we collected qualitative feedback from residents about the clinical experience and knowledge gaps in order to improve the educational content. Based on this feedback, we formalized the rotation objectives and created a 60-minute interactive lecture on the following overarching topics: the evolution of telemedicine, common telemedicine delivery modalities, technological aspects, licensure, reimbursement, the teleneurologic examination (table e-1, doi.org/10.5061/dryad.4j9n25d), "website manners" (table e-2, doi.org/10.5061/dryad.4j9n25d), telemedicine challenges, and future applications.

In July 2017, we launched the updated, more formalized curriculum along with the current quantitative study in the PGY3 and PGY4 residents starting their rotation. Precurriculum assessments were given prior to the start of the rotation, which began with the one-on-one interactive lecture delivered to each resident by the authors. Postcurriculum assessments were given following the completion of their first 2-week block to standardize assessment timepoints for all residents. All assessments were voluntary, anonymous, de-identified, and administered electronically and stored through a RedCAP database. Only pooled data were reviewed and analyzed at the completion of the study period to preserve...
Outcomes

Our primary outcomes were to assess the change in residents' (1) telemedicine knowledge base, (2) perspectives on telemedicine video visits compared to in-person visits, and (3) perspectives on the challenges and benefits of telemedicine, as assessed by comparing precurriculum and postcurriculum quizzes and survey responses, respectively. Our secondary outcomes pertained to residents' self-assessed competence in telemedicine skills, as well as perceived value of telemedicine training.

Statistical analysis

A paired t test was used to compare quiz scores before and after the rotation. Data collected on residents' perspectives towards telemedicine demonstrated a nonparametric distribution, thus a Wilcoxon signed rank test was used to compare matched data points precurriculum and postcurriculum. A significance level of 0.05 was used for all tests. All statistical tests were performed using Microsoft Excel, version 16.17 (Redmond, WA).

Data availability

The full set of de-identified data is available upon request.
Table Components of teleneurology survey questions

<table>
<thead>
<tr>
<th>Comparing video visits to in-person visits</th>
<th>Challenges of teleneurology</th>
<th>Benefits of teleneurology</th>
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<tr>
<td>How do video visits compare to in-person visits with respect to the following aspects of a typical patient visit?</td>
<td>How much of a challenge do you believe the following factors are for the practice of teleneurology?</td>
<td>How much of a benefit do you believe the practice of teleneurology provides for the following factors?</td>
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<tr>
<td>1. Identifying patients’ chief concerns</td>
<td>1. Patient’s lack of interest</td>
<td>1. Reducing travel time for patient</td>
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<tr>
<td>2. Obtaining a focused history</td>
<td>2. Provider’s lack of interest</td>
<td>2. Reducing overall burden of clinic visit for patient</td>
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<tr>
<td>4. Communicating recommendations</td>
<td>4. Provider’s ability to make a personal connection</td>
<td>4. Reducing costs for patient</td>
</tr>
<tr>
<td>5. Establishing a personal connection</td>
<td>5. Provider’s ability to perform a neurologic examination</td>
<td>5. Reducing costs for providers/health systems</td>
</tr>
<tr>
<td>6. Overall quality of care provided</td>
<td>6. Provider’s ability to make an adequate assessment</td>
<td>6. Improving access to care for rural/remote patients</td>
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<td>14. Documentation</td>
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Results

Primary outcomes

Telerehabilitation knowledge

All residents improved in their quiz performance, and on average, scores improved from 53.3% on the precourse quiz to 88% on the postcourse quiz with a median score increase of 8 points on the 26-point quiz ($p = 0.002$) (table e-3, doi.org/10.5061/dryad.49n25d for quiz).

Perspectives on video visits vs in-person visits

Following 2 weeks of the telerehabilitation rotation, residents’ impression of video visits compared to in-person visits changed, with more residents indicating video visits to be the “same” if not “somewhat superior” to in-person visits with regards to 4 of 6 factors surveyed, obtaining a focused history, formulating a focused assessment and plan, communicating recommendations, and the overall care provided ($p < 0.04$) (figure e-1, doi.org/10.5061/dryad.49n25d). No statistically significant difference was seen for identifying patients’ chief concerns (all residents identified this as “same” at both timepoints; $p > 0.99$) and establishing a personal connection (all residents identified video visits to be the “same” or “somewhat inferior” to in-person visits; $p = 0.20$).

Perspectives on the challenges and benefits of telerehabilitation

A statistically significant difference was seen in residents’ perspectives on the challenges of telerehabilitation practice following 2 weeks of the rotation in 3 of 14 obstacles surveyed. Residents perceived less challenge in performing a neurologic examination ($p = 0.02$), making an adequate patient assessment ($p = 0.02$), and navigating technological barriers ($p = 0.04$) (figure e-2, doi.org/10.5061/dryad.49n25d). Many residents recognized that reducing travel time, overall burden of the clinic visit, and costs for the patient were clear benefits even prior to the rotation. However, after 2 weeks of the rotation, residents’ perspectives on the benefit of reducing caregiver burden specifically changed; 90.9% of participants identified this as a “major benefit” after, compared to only 54.6% before the rotation ($p = 0.04$).

Secondary outcomes

All residents indicated feeling more competent using telerehabilitation for patient care in their eventual career after completing 2 weeks of the rotation. Of note, residents saw, on average, between 11 and 20 patients on their rotation, with an upper range of 21–30 patients. All residents either agreed or strongly agreed with the statement, “I feel comfortable conducting a telerehabilitation patient video visit.” A total of 90.9% of
residents either agreed or strongly agreed with the statement “Overall, I feel that formal training in telemedicine applications and practice is a useful and/or needed aspect of neurology residency training.”

Discussion

As telemedicine becomes a major component of neurologic care, future outpatient neurologists will need to be proficient in delivering specialized care through a virtual platform. This study provides evidence for the benefits of formally implementing a basic telemedicine curriculum for neurology residents in outpatient clinics. Our study found that neurology residents found the formalized training in the growing field of tele-neurology valuable. Following an interactive lecture and just 2 weeks of exclusively tele-neurology hands-on clinical experience, residents’ knowledge of core telemedicine topics grew significantly, and there was a positive shift in residents’ perspectives on aspects of telemedicine that often receive criticism (e.g., the ability to perform an accurate neurologic examination and assessment). Many benefits of telemedicine were already perceived as such prior to curriculum, but with hands-on experience, residents noted the importance of caregiver support when it comes to many neurologic patients, and recognize the opportunity video visits present for this patient population.

Residents indicated that video visits are inferior to in-person visits in “establishing a personal connection” with patients. This is consistent with the often-identifed concern about de-personalization of the provider-patient relationship and the AAN Telemedicine Work Group’s recommendation that tele-neurology curriculums should cultivate “webside manners” and emphasize that telemedicine is a means to enrich in-person care, not replace it (table e-2, doi.org/10.5061/dryad.4j9n25j).

We recognize the small sample size and lack of control group are major limitations in this study. Furthermore, while the neurology faculty evaluations of the residents on this rotation were uniformly positive, competence in tele-neurology skills was only self-assessed at the end of the first 2-week block. Our clinical rotation provided a strong clinical experience in diverse outpatient general and subspecialty neurology clinics, but lacked any exposure to inpatient or emergency consultations, such as telestroke. Similarly, while residents perceived the tele-neurologic examination as overall less challenging following the curriculum, we did not analyze how this differed between subspecialties (e.g., a thorough neuro-muscular examination may be more limited than a movement disorders examination). This is where further discussion of specific clinical vignettes and troubleshooting techniques with a seasoned subspecialist, as the AAN Telemedicine Work Group has outlined, could have added benefit even in an experiential curriculum.

This curriculum was developed at a single academic center, tailored to needs, funding, and feasibility within the UCSF neurology residency program, and implemented at SFVAMC with its already robust telemedicine infrastructure and expertise. Each institution should tailor their tele-neurology education to their capabilities. For instance, though our curriculum shares several of the themes and core competencies outlined by the AAN, it focuses more on developing comfort in outpatient tele-neurology through experiential training over didactics. Having said this, the modules and vignettes the AAN has outlined are appropriate alternatives to fill the gaps where local expertise or feasibility of telemedicine encounters is not available at any given institution. In our next iteration of this curriculum, we hope to enhance this curriculum with case-based discussions and a journal club.

This curriculum may serve as a basic pilot experiential-based outpatient tele-neurology curriculum that together with the AAN Telemedicine Work Group’s curriculum recommendations could lay the groundwork for the development of tele-neurology curricula in residency programs across the country. Future efforts should include the development of best education practices and assessment of patient and caregiver satisfaction with resident video visits in this ever-evolving field.

Study funding

No targeted funding reported.

Disclosure

The authors report no disclosures relevant to the manuscript. Go to Neurology.org/N for full disclosures.

Appendix Authors

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- You can include a maximum of five authors (including yourself)
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 & Fellow Section editor before submission to inquire about the need for an article on a particular topic.
Emerging Subspecialties in Neurology: Medical education

Patrick M. Chen, MD, and Sean J. Evans, MD


Abstract

Medical education is the understanding of how medical knowledge is taught and practiced and encompasses not just medical students, but resident trainees, colleagues, and the community. While there is a growing emphasis in medicine on "clinician-educators," neurology training has only slowly developed formal opportunities in medical education. Here we highlight the current opportunities in residency and beyond, and explore options for further medical education infrastructure within neurology.

The need for medical educators in neurology

While an aging population and expanded therapeutics are driving demand for neurologists, neurology is ill-equipped to meet this growing need. One reason is neurophobia, a "fear of the neural sciences and clinical neurology ... due to inability to apply their knowledge of basic sciences to a clinical situation." Neurophobia is well-documented in students and generalist practitioners globally. A lack of formal education, general misunderstandings, and lack of strong neurologic role models are proposed explanations. A recent article by Lin et al. in Neurology® highlights challenges clinician-educators face and notes the need for good educators in a progressively complex field to protect and incentivize the "art of neurology."

Formalized medical education can combat neurophobia and internal burnout. We note that the term "burnout" is frequently used in the press though it is still an unestablished entity under investigation. We propose a "ground up approach": develop medical educators who are role models and leaders, then update and enrich curriculums, inspire trainees, and empower them to engage meaningfully with neurology. Better trained students will help deter burnout in our residents and help remove neurology from its position in the top 5 specialties for regret and burnout.

While education of future neurologists is a core element of our profession, training educators has been a passive process with little formal curricula. This needs to change.

The role of residents in medical education

The resident is at the forefront of clinical teaching for medical students, serving as both near-peer and role model. One third of a medical student's fund of knowledge is acquired from resident teaching. The magnitude and importance of education is often at odds with the limited formal educational training provided to the neurology resident. The formal development of medical teaching skills is not an explicit requirement of programs in the Accreditation Council for Graduate Medical Education (ACGME) requirements. Although residents may spend up to one-fourth of their time supervising or teaching students and co-residents, the ACGME neurology milestone project places education vaguely and more broadly under "scholarly activity." The onus for structure therefore lies on the program and resident. Many programs center the role of education on the senior resident, assuming that seniority is equal to apt teaching ability, which may be
a fallacy. In addition to conveying knowledge, residents perform educational administrative responsibilities: observation, formative assessments, and summative evaluations. A resident, juggling many tasks, may easily provide teaching suffering both in quantity and quality.

Residency program directors need to adopt their curricula to prepare all neurology residents for their role as educators, and need to demonstrate how teaching students reinforces residents' core knowledge, potentially producing happier, more successful residents who become happier, more successful neurologists.

Training opportunities in neurology residency

All neurologists need to effectively educate their patients, their colleagues, and their own trainees. In current practice, residents often self-direct their learning of medical education. Residents should familiarize themselves with basic educational theories and how they underpin teaching techniques. Trainees interested in developing a curriculum of self-learning may be interested in "5 Microskills for Clinical Teaching" and resources provided by the Association of American Medical Colleges (AAMC) MededPORTAL, Journal of Graduate Medical Education, and New England Journal of Medicine Resident 360 Section.

A study showed that "resident as teachers" curricula (residency integrated programs focusing on teaching) significantly improve teaching abilities, reinforce resident knowledge, and bolster postresidency placement. Accordingly, neurology training programs (e.g., UCLA, Yale) are beginning to offer longitudinal clinical-educator tracks (combining didactic series, education electives, leadership of small groups, bedside teaching, and mentored scholarly projects) within the residency. Ideally those developing educational tracks will reflect the AAMC's findings that relationship-based, noncognitive skills are a core feature of effective teaching, and include enhancement of a resident's "softer" skills, including leadership by example, teacher-student communication, and providing feedback, not just theoretical knowledge.

Opportunities for application of resident teaching skills are varied, including serving as teaching assistants for anatomical dissection, facilitating practicums, and providing a link between basic science and clinical application, bringing preclerkship material to life. Residents may serve as leaders of small group sessions in both preclerkship and clerkship level courses. Utilization of simulation training in neurology allows residents to serve as proctors in structured settings. Our program recruits and prepares neurology residents to engage in these opportunities in the preclerkship and clerkship level curriculum while encouraging them to engage medical students as active learners. Helping students to explain their thought process and apply their knowledge is critical, and by flipping classrooms, replacing lectures with small group and team didactics, and adding clinical simulations, training programs can enrich residents with educational exposures, allowing them to experiment and innovate in medical education. In addition, engaging residents to ask practical research questions about assessments, simulations, and the effect of quality improvement on clinical competency will allow them to take advantage of formal research grants funding innovative medical education projects provided by the American Academy of Neurology (AAN) Education Research Grant, AAMC, and National Board of Medical Examiners (table).

Postgraduate training opportunities

Most neurology residents enter fellowships to develop specialized skills in both application and research within a field of interest. It seems logical that similar subspecialty training would be created for future neurologic educators, and indeed, other fields have created multiple such programs. Emergency medicine leads creation of postgraduate education opportunities with 30 nonmatch fellowships. These programs vary, but typically are 1–2 years, split clinical attending duties with dedicated didactics (curriculum design, research methods), and eventually result in journal publication, grant application, or master's degree attainment.

Within neurology, medical education fellowship opportunities remain limited. A number of articles lament the difficulty of using T-32 or R25 grants in fellowship toward a clinician educator path. A review of Google (search terms: "neurology medical education fellowship," "neurology education fellowship"), the AAN fellowship directory, ACGME, and United Council for Neurologic Subspecialties databases showed only 1 neurology-specific education fellowship. The AAN Institute Medical Educator fellowship is a research-based stipend fellowship for AAN members who have completed neurology/child neurology or neurodevelopmental disabilities residencies or fellowship in the last 5 years. A $65,000 stipend is provided to pursue "medically oriented education research." The fellowship's focus is on research to develop behavioral and psychosocial interventions in "teaching, learning and health care practice," with an overarching goal of improving patient and family outcomes.

Do formalized fellowships create better medical teachers? There are little outcome data to provide an answer. Preliminary studies show these tracks are feasible, and graduates think positively of the programs. These fellowships have worth, even in early days, because they codify medical education as a scholarly career, worthy of aspiration. It is intuitively appealing that these programs will make a trainee a better teacher, and they create the expectation that medical education is an active and multifaceted career option.

In the interim, integrating medical teaching skills into existing fellowships is appealing. Possibilities in fellowship include fellows partnering with attendings in ward teaching,
Table Abbreviated list of medical education-specific research grants

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<tr>
<th>Grant name</th>
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<tr>
<td>American Academy of Neurology Education Research Grant</td>
<td>tools.aan.com/science/awards/?fFuseAction = home.info&amp;aid = 48</td>
<td>Provides support for qualitative or quantitative study of hypothesis-driven observation or interventions on knowledge acquisition or training. Grants include improving current American Academy of Neurology programs and the study of trainee educational programs. Trainees are not eligible.</td>
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<td>Steimler Medical Education Research Fund</td>
<td>ribme.org/research/steimler.html</td>
<td>Supports research and development of innovation in the evaluation of preparing and practicing medicine. Broad topics of interest include theory, knowledge, and practice assessment in medical education. Collaboration is encouraged.</td>
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<td>To encourage and support research addressing important problems in medical education. Areas include faculty development, learning environment, and interprofessional. Applicants must be a GEA affiliated institution. Collaboration among other regional GEA sections is encouraged.</td>
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<td>Regional GEA sections providing funding for medical education research scholarship and evaluation.</td>
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Abbreviations: AAMC = Association of American Medical Colleges; GEA = Group on Education Affairs.

protecting fellow time to work with resident level trainees, and incentivizing specialty-specific education research.

Finally, educationally geared faculty development programs are provided by some academic centers, and fellows or attendings can pursue a master’s degree or PhD in medical education, clinical education, or education. This is a formalized, but intensive route, and it is unclear to what degree it is in addition rewarded.

**Clinician educator and practice models post-training**

Breaking from traditional emphasis on research alone, academic centers are increasingly hiring clinician educators. A number of reasons are cited for this change, including competitive research funding, increased numbers of trainees, and increased clinical care needs.7

The acceptance of the clinician–educator is seen in clinical professorship tracks. Promotion criteria on these tracks vary, but generally require longitudinal dedication to teaching activities and mentorship, with demonstration of quality and quantity of teaching exceeding that of peers. Certain institutions have begun to grapple with the challenges of financially incentivizing teaching by developing an educational relative value unit (RVU) system. The RVU system is a scale to adjust payment by intensity of clinical resources used for provider–patient interactions. Educational RVUs would analogously assign monetary value to teacher–learner interactions.12 This incentivization on a national level is imperative to elevating the role of clinician-educators.2 Financially supported educational leadership positions include the predeakship course director, deakship director, residency program director, and roles within Medical Education administration. Uncompensated but meaningful opportunities to affect neurology education include service on standard setting subsections at national meetings and developing test material for licensure with the National Board of Medical Examiners, American Board of Psychiatry and Neurology, and a variety of subspecialty entities.

Medical education is a rapidly growing field in neurology, but is still young. We describe the current landscape of opportunities in medical education, and at present, due to few formal training opportunities in neurologic medical education, place the onus on self-motivated residents to explore their interest in teaching, and to enhance their abilities as educators. Opportunities to develop formal neurology education curricula and to support dedicated postresidency fellowships abound. Neurology should keep pace with other fields in advancing current and future clinician-educators.

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Global and Community Health

More than 85% of the world’s population lives in low and middle income countries, where the burden of neurologic disease is greatest. In addition, over 50 million Americans live in medically underserved communities. Despite these figures, relatively little is known about patients and practitioners of neurology in resource-limited settings. This section aims to explore global and community health topics in neurology education. We welcome manuscripts describing international educational exchanges, personal rotations in low and middle income countries, and work by neurology trainees from around the world. We also welcome manuscripts that discuss community health initiatives and volunteer experiences in underserved regions of the United States. Inclusion of practical information on local or international volunteer opportunities would also be of use.
Global & Community Health: A perspective on neurologic care at Mulago Hospital in Uganda

Monica M. Diaz, MD

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Looking out from atop Uganda National Mosque’s minaret, one of the highest points in Kampala, the capital city of Uganda, one sees winding narrow roads turning bright orange with rainfall converging to meet at the mosque in Old Kampala. These roads are congested with a lawless swirl of traffic involving pedestrians, matatus (communal taxis), and boda-bodas (motorbikes). There are women in colorful gomesis (traditional dress in the Buganda kingdom), men in dress shirts, and children selling fruit on the side of the roads, all working under the heat of the equatorial sun to bring life to this beautiful, chaotic city. As a resident in my second year of neurology training, I had the opportunity to visit and participate in care for this Ugandan community. I spent 6 weeks in Kampala on an international elective rotation coordinated through the Yale/Stanford Johnson & Johnson Global Health Scholars Program at Mulago Hospital, an experience that enhanced my training as a neurologist and perspective as a clinician.

Uganda is a country of 39 million people with 40 spoken dialects, sitting on the shores of Lake Victoria in East Africa. It has earned the title of “The Pearl of Africa,” with its lush vegetation, copious rainfall, and abundant wildlife. Despite these natural resources, only 26.7% of the population, mostly in urban areas, has access to electricity.1 Almost half of the population is under the age of 15, with a life expectancy of 59 years, and the average fertility rate is 6 children per Ugandan woman.2 Despite this, Uganda has reduced monetary poverty at a rapid rate, from 31.1% living below the national poverty line in 2006 to 19.7% in 2013.3

My experience in Kampala, Uganda, began on the neurology wards of Mulago Hospital, a public 1,500-bed facility that attends to 120,000 inpatients annually as the main tertiary referral center in Uganda. Each day we saw about 30-40 patients, all housed within 2 large rooms, divided into male and female wards. Hospital beds were pressed up next to each other, draped with colorful blankets brought from home (the hospital does not routinely provide sheets), without divider curtains as a refuge for privacy. The nurse to patient ratio is about 1 nurse to 20-30 patients. An attendant (or caregiver who accompanies the patient from their home village) sits by the bedside on a straw mat and provides the most basic patient care, from toileting, feeding, and washing bed sheets, to going to pharmacies to purchase inpatient medications, to dispensing the medication to the patient.

The day begins with bedside rounds each morning with a hospitalist attending physician, a senior house officer (or resident), intern, and medical students. The hospital provides patient charts that are kept at bedside during their inpatient stay, which patients and attendants retain after discharge from the hospital. The patient is examined, the chart is reviewed on rounds, and a plan is formulated at the bedside. Much of the time is spent explaining the costs of medications, procedures, or imaging studies to the patient and attendant, as costs tend to be the factor that decides what care the patient can receive.

Only 2% of Ugandans have private health insurance; thus, the majority of personal health care expenses are paid out-of-pocket in cash at the time of hospital admission. Although health care in Uganda is free, patients must pay most expenses out-of-pocket in cash if not covered by the national health care system. Those who cannot pay must borrow money from family or sell...
possessions or petition the hospital to pay for their hospital stay.\textsuperscript{4,5} It is common for patients to spend 3–4 days in the casualty (or emergency department) prior to admission to the neurology ward. Few tests are provided for free, including complete blood count testing, immune suppression syndrome (the name given to HIV in Uganda) testing, chest X-ray, and lumbar puncture. A brain CT scan costs $100 USD and an MRI brain about $500 USD, and many patients cannot afford either. Mulago Hospital houses 2 CT scanners, both of which were nonfunctioning during my time there, so patients were referred to private hospitals to obtain a CT scan, sometimes using the hospital ambulance but often transported in a family member’s personal vehicle. Four EEG machines are available, but there may not be personnel trained to read and interpret EEGs. Lumbar punctures are often performed once increased intracranial pressure is ruled out via a funduscopic examination (CT scans could take days to obtain). Critical care is limited. A 5-bed intensive care unit (ICU) exists in Mulago Hospital but beds are always occupied. A patient presenting in an obtunded state would have quickly been intubated and moved to a higher level of care in the Western world, but this is simply not possible without access to a ventilator and ICU. Patients in respiratory distress are placed on their side to prevent aspiration with an emergency oral airway in place, and the patient is connected to an oxygen tank shared with 5 other patients also in respiratory distress. Despite these drawbacks, Uganda has made advances in palliative care services, with nurses trained in assisting with end-of-life care on the wards.\textsuperscript{5}

Because many resources are either not available or unable to be paid for, much of the assessment relies on the neurologic history and examination. The neurologic history is at times limited by a language barrier, with an attendant of another patient who speaks the patient’s dialect often serving as interpreter. The neurologic examination is crucial given limited imaging studies available. A patient with HIV presenting with hemiparesis has either toxoplasmosis or a stroke until proven otherwise, and if no head CT can be obtained, then the patient is discharged on aspirin for stroke prevention and empiric toxoplasmosis treatment. Patients presenting obtunded and febrile with anemia are treated for cerebral malaria. A diagnosis of atrial fibrillation in a stroke patient is made by palpation of the radial pulse, and elevated intracranial pressure is ruled out by funduscopic examination. I evaluated patients with illnesses common in the United States, such as hemorrhagic and ischemic strokes, seizures, myasthenia gravis, Parkinson disease, and spinal cord compression. I also cared for patients with conditions less prevalent in the United States, such as toxoplasmosis, progressive multifocal leukoencephalopathy, tuberculous meningitis, neurocysticercosis, and cerebral malaria. Much of the infectious diseases ward contained patients with HIV-related opportunistic infections, meningitis, and tetanus (mostly unvaccinated people who had stepped on a nail and developed trismus, laying in beds under a black cover used to reduce stimuli). Many patients are discharged without a definitive diagnosis without the benefit of neuroimaging or EEG. The hospital provides few select medications for free, but in most instances, the required medications, which often are unaffordable, must be paid for in cash by the patient and patient’s family. Available antiepileptic drugs include phenobarbital, carbamazepine and phenytoin, but antiepileptic drug levels are unavailable. Aspirin and antihypertensives are available for stroke prevention. IV mannitol may not be available in the hospital pharmacy and must be purchased from an outside pharmacy by the attendant.

Neurologic care in sub-Saharan Africa is often limited by the cultural stigma surrounding neurologic illness, scarcity of medications, inability to pay for tests, and inaccessibility to specialists. Neurologists are scarce throughout sub-Saharan Africa, with 1 neurologist for every 4 million people.\textsuperscript{5} Mulago Hospital has 1 neurologist on staff and most neurologic care is provided by internists. The role of a visiting neurology resident in a limited resourced setting can be unclear at times, but one important way to foster interest in neurology is to provide teaching of clinical neurology and neurologic examination findings to the local residents and medical students. Raising awareness of the importance of specialty training in neurology will help create a stronger interest in the field of neurology among Ugandan trainees, subsequently making a plea for development and funding of local neurology training programs. Neurology trainees can help by participating in an international rotation in an underresourced country. The Yale/Stanford Johnson & Johnson Global Health Scholars program is available to internal medicine and emergency medicine residents in the United States, and was coordinated for neurology residents with the help of faculty in the Yale Department of Neurology and Makerere University in Kampala. The program has also sponsored visiting physicians from other countries to spend up to 1 year rotating on the neurology wards at Yale. The goal of programs such as these is to help achieve equality in medical as well as neurologic care throughout the world. Recently, a stronger interest has been expressed in global neurology exchange programs, many of these with long-standing exchange partnerships that help foster collaboration and education between the institutions.\textsuperscript{6} My Ugandan colleagues taught me how to diagnose infectious diseases underrecognized in the United States without the use of ancillary diagnostic tools, and shared a wealth of knowledge with me. My experience at Mulago Hospital was invaluable as it helped not only to refine my clinical skills as a neurologist, but also helped me to see neurology from a humble perspective.

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We thank Dr. Gross for his support of the Resident & Fellow section. He has enthusiastically embraced the section and our many initiatives over the past 10 years. We wish him well as he finishes up his term.

Have some fun!
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 NPub.org/aheadofprint 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 three-year residency cycle. Submissions should be timely and are requested no longer than four 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: Association between aspirin dose and subarachnoid hemorrhage from saccular aneurysms

A case-control study

Shashank Agarwal, MD, Ting Zhou, MD, and Jennifer Frontera, MD


Risk factor modification is important in the prevention of aneurysmal subarachnoid hemorrhage (aSAH) in patients with unruptured aneurysms. Currently there are conflicting data on the role of antiplatelet and antithrombotic agents in the prevention of aSAH. Recent studies and meta-analyses show mixed findings, with some suggesting that the use of aspirin is associated with increased risk of aSAH and others demonstrating protective effects.4

The study by Can et al.4 contributes to this ongoing debate. This Journal Club discusses the study's strengths and weaknesses. The authors concluded that aspirin therapy at diagnosis was associated with a significantly decreased risk of aSAH, with an inverse dose–response relationship among aspirin users. However, once ruptured, aspirin is associated with an increased risk of re-rupture before treatment. Since prior studies have revealed a conflicting role of aspirin in the prevention of aSAH, it is imperative to discuss the findings of this study through a journal club.

Hypothesis and design

The authors sought to address the following questions: (1) Is there an association between aspirin use and aSAH? (2) Is there an association between aspirin dose and aSAH? (3) What is the association between aspirin use and re-rupture risk in patients with an untreated intracranial aneurysm?

This was a case-control study consisting of 4,701 patients and 6,411 aneurysms, and incorporated both cross-sectional data from retrospective chart review and prospectively collected data on a subgroup of patients.

Methods

The study first included a total of 6,063 patients with both retrospectively (4,862) and prospectively (1,201) collected data from the Partners Healthcare Research Patients Data Registry, as well as from datasets at the Brigham and Women's Hospital and Massachusetts General Hospital. The authors then reviewed the medical records and imaging studies to ultimately identify 4,701 patients with 6,411 definite saccular aneurysms. Presumably all identified aneurysms were both intracranial and intradural, though the authors do not specify if they excluded patients with cavernous carotid aneurysm, superior hypophysemal, or other intracranial extradural aneurysms. The authors also do not specify how many of these patients had prospective data compared to cross-sectional data at the time of presentation, nor do they specify the number of patients with unruptured aneurysms who were prospectively followed. The authors then divided these patients into 2 groups: disease group with ruptured aneurysms and
control group with unruptured aneurysms. They then evaluated the association of exposure to aspirin therapy with aneurysm rupture status at presentation.

Analysis of the differences in the baseline characteristics between the 2 groups was done using t tests for continuous and Pearson χ² tests for categorical variables. It is unclear why the authors did not utilize nonparametric analyses for data that are not normally distributed. To evaluate the association between aspirin use/dosage and subarachnoid hemorrhage (SAH) from saccular aneurysm, the authors used univariable and backward stepwise, multivariable logistic regression models. Sensitivity analysis was conducted to examine if results in all patients with antplatelet therapy were different from those with aspirin use.

Results

Of the 4,701 patients with saccular aneurysms, 4,102 patients were not taking any antplatelet drugs, whereas 599 were on antplatelet therapy. Of the patients on antplatelet therapy, 517 were on aspirin and 82 were on nonaspirin antplatelet medications. A total of 1,302/4,701 (28%) patients had aSAH. Overall, patients on aspirin therapy were significantly older and were less likely to present with SAH. In addition, patients on aspirin therapy were less likely to be current smokers but more likely to have coronary artery disease, myocardial infarction, atrial fibrillation, or hypertension, as well as to be taking antihypertensive medications. In weighted multivariable analysis, black race (odds ratio [OR] 2.03, 95% confidence interval [CI] 1.42–2.91), Hispanic race (OR 1.82, 95% CI 1.18–2.81), Asian race (OR 2.86, 95% CI 1.39–5.86), and current alcohol (OR 2.07, 95% CI 1.60–2.68) and tobacco use (OR 1.39, 95% CI 1.09–1.78) were significantly associated with aSAH, whereas aspirin use (OR 0.65, 95% CI 0.53–0.81) and female sex (OR 0.64, 95% CI 0.49–0.84) correlated with lower risk of aSAH. Higher aspirin dose (unweighted OR 0.72, 95% CI 0.60–0.85, weighted OR 0.65, 95% CI 0.53–0.81) was also significantly associated with decreased risk of aSAH. In a small subgroup of patients (n = 17) with aneurysm re-rupture (4 were on aspirin at the time of rupture), aspirin therapy was significantly associated with increased risk of re-rupture. Sensitivity analysis showed that the results for patients on all antplatelet therapy were not any different from patients on only aspirin.

Discussion/interpretation

The major strengths of this study include the use of machine learning algorithms and manual review of medical record and imaging data to identify patients from the organization registries and electronic medical records, which is likely much more reliable than diagnosis codes alone. Another strength of the study was the sensitivity analysis that demonstrated similar results among patients with aspirin or the use of any other antplatelet agent.

Though the authors have done well to select a population of patients with unruptured intracranial aneurysms as the control group, there are some major limitations to the study design. First, it is unclear why patients with unruptured aneurysms presented in the first place, whether these aneurysms were incidental findings or generated symptoms leading to presentation. Second, a true control group would include a random sampling of an age-matched population of patients with unruptured intracranial aneurysms in the community, not merely patients who presented to the hospital or clinic and were found to have an unruptured aneurysm (selection bias). Though the authors attempt to identify and control for differences between those with ruptured vs unruptured aneurysms through propensity-weighted score matching and multivariable analysis, these do not account for lead time bias such that patients with unruptured aneurysms present earlier in the disease course and may have not been exposed to a rupture risk for as long as those who presented with aSAH. Not knowing the duration of time an aneurysm is present, and hence the time frame of risk exposure, makes it a significant limitation of this study and substantially mitigates against any conclusions that can be drawn about other exposures contributing to rupture (including aspirin use).

Overall, this study demonstrates that aspirin use is more common in patients who present with unruptured intracranial aneurysms than those who present with SAH. However, without knowing the time course of disease, it is impossible to conclude that aspirin reduces the risk of aneurysm rupture (since risk is inherently measured over time). Instead, it is possible that aspirin use among patients with cardiovascular disease (as in this cohort) increases the risk of undergoing a vascular study that reveals an incidental unruptured aneurysm. A preferable study design would have been one in which the authors presented their prospective data following patients with unruptured intracranial aneurysms who were or were not exposed to aspirin and then reported on the rate of aneurysm growth and rupture stratified by aspirin use.

Other limitations include the fact that the duration of aspirin or antplatelet exposure was not identified in this study. While several studies suggest that inflammation is linked to aneurysm formation, growth, and rupture, short-term use of an antplatelet agent does not plausibly reduce inflammation-mediated aneurysm rupture. Further, since it is unclear why those with unruptured aneurysms came to medical attention, it is possible that headache related to an unruptured aneurysm led to short-term aspirin use.

Both hypertension and smoking are associated with an increased risk of aneurysm rupture. Aspirin users had lower rates of smoking and higher rates of antihypertensive medication use. Though this does not tell us about blood pressure control among aspirin users, it may represent a marker for better medical care in this group. Other important risk factors for aneurysm rupture are aneurysm size and the location of aneurysms, which were not accounted for in this study. The
authors did report size of the largest aneurysm but it does not inform about the average size of aneurysms in each group.

When evaluating the association of aneurysm re-rupture and aspirin use, the authors did not account for factors that affect re-rupture risk such as admission Hunt–Hess score, aneurysm size, or the use of antifibrinolytic agents. Furthermore, the authors report a low 1% rate of aneurysmal re-rupture (17/1,302), compared to the 7%–17% risk that has been reported in several cohorts. This leads one to believe that re-rupture rates were overall under-reported and that there may have been a reporting bias such that aspirin use may have been more frequently documented among those that re-ruptured.

The conclusion that can be drawn from these results is that the prevalence of aspirin use at the time of presentation is higher in patients with unruptured aneurysms than in those with aSAH. Data are lacking on how long these patients harbored the aneurysms or the duration of their aspirin therapy. Due to these limitations, it is not possible to draw conclusions about the use of aspirin and the risk of aneurysm rupture. We suggest that the element of time is critical to study design when evaluating risk and the true effect of antiplatelet therapies would best be evaluated prospectively or in a randomized study.

Author contributions
S. Agarwal: drafting/revising the manuscript, analysis or interpretation of data, accepts responsibility for conduct of research and final approval. T. Zhou: drafting/revising the manuscript, accepts responsibility for conduct of research and final approval. J. Frontera: drafting/revising the manuscript, analysis or interpretation of data, accepts responsibility for conduct of research and final approval, study supervision.

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References

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Mystery Case

Interesting teaching cases submitted to the Resident & Fellow Section are chosen by the 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 one to three questions. Responses are compiled and then published with the full case.
Mystery Case: A 23-year-old man with headaches, confusion, and lower extremity weakness

Nikhil M. Patel, MD, Jay Bronder, MD, Melissa Motta, MD, and Nicholas Morris, MD


Section 1

A 23-year-old man was found at a train station with convulsions. He was treated with benzodiazepines in the field and transferred to the nearest emergency department, where he was intubated. This episode had been preceded by a 2-week history of headaches, nausea, confusion, and staring spells that precluded the patient from going to work. His mother also noted that his eye started to appear “droopy” several days prior to presentation. She stated that he had no recent travel, sick contacts, or tick or insect bites. He was recently prescribed and had been taking acetaminophen/butalbital/caffeine for symptomatic relief of his headaches but was not taking any other medications. He was admitted to an outside hospital and subsequently transferred to our facility.

The patient’s examination on arrival was notable for eye opening to sternal rub. He had a right eye ptosis with no extracocular or pupillary abnormalities and a left facial droop without forehead involvement. He had symmetric weakness in his lower extremities (1/5) more than his upper extremities (3/5). Tone was noted to be normal throughout, and reflexes were noted to be 2+ in biceps, brachioradialis, triceps, and patella bilaterally. Ankle jerks were noted to be absent, with downgoing plantar response bilaterally.

Questions for consideration:
1. How would you localize this patient’s symptoms and presenting examination?
2. What is your differential diagnosis at this time?
3. What additional workup would you recommend?
Section 2

The patient's convulsion as well as previous staring spells raises the suspicion of seizures, which along with his headaches and altered mental status points to a lesion in the brain or meninges. Accompanying nausea indicates the possibility of elevated intracranial pressure.

The presence of a ptosis without ophthalmoplegia, pupillary abnormalities, or other cranial nerve (CN) findings makes a nuclear or fascicular lesion unlikely, and points to a lesion involving the superior division of the oculomotor nerve. A basilar meningitic process could cause a CN III lesion but would be unusual to manifest as isolated ptosis. A lesion in the cavernous sinus, in the form of a thrombosis or infiltrative lesion, is unlikely given the lack of extraocular movement abnormalities or indication of a lesion of the ophthalmic division of the trigeminal nerve. Horner syndrome should be accompanied by pupil enlargement, although this can be subtle. A microvascular lesion of CN III is extremely unlikely in a young patient with no vascular risk factors. Myasthenia gravis is frequently associated with ptosis and while it can often be asymmetric, it is usually bilateral and associated with some diurnal variation and fatigability. Miller Fisher variant of acute inflammatory demyelinating polyradiculoneuropathy (AIDP) can be accompanied by ptosis but is usually not asymmetric and unlikely to cause seizures and alterations in mental status. An orbital lesion, either a myositis or an infiltrative process, is possible and could explain ptosis without pupillary or extraocular abnormalities.

The facial droop without forehead involvement suggests an upper motor neuron lesion above the level of the mid-pons. The patient's motor examination was notable for symmetric lower greater than upper extremity weakness. Classically this is consistent with a central cord syndrome, and commonly presents with cape-like sensory deficits of pain and temperature due to involvement of the deusarting spinthalamic tract fibers in the anterior commissure. However, there is no sensory level or other sensory abnormalities to further localize the lesion at this point. Overall, the constellation of signs and symptoms localizes to a multifocal CNS process involving the brain, brainstem, and spinal cord or a meningitic process.

With this in mind, the differential diagnosis remains broad. Infectious causes such as viral or fungal meningitis are possible given the acute to subacute nature of the patient's symptoms. While the time course makes most causes of bacterial meningitis unlikely, some pathogens to consider are Borrelia burgdorferi (Lyme), Ehrlichia, Bartonella, Brucella, and Rickettsia species. Possible viral etiologies include RNA viruses such as HIV, enterovirus or Coxsackie virus, flaviviruses such as West Nile virus or Zika virus, and herpes family viruses such as herpes simplex virus or varicella-zoster virus. Other herpes family viruses such as cytomegalovirus, Epstein-Barr virus, human herpesvirus (HHV)-6, and HHV-7 should be considered in immunocompromised states. Endocarditis with multifocal septic emboli and multifocal abscess should also be considered. Inflammatory causes to keep in mind are neurosarcoidosis, systemic lupus erythematosus, Sjögren syndrome, and CNS vasculitis (either primary or as part of a systemic process). A demyelinating condition such as acute disseminated encephalomyelitis (ADEM) or neuromyelitis optica (NMO) could also explain the clinical presentation.

Initial laboratory results were notable for hyponatremia of 127 mEq/L and white blood cell count of 9.4. Lumbar puncture revealed a pleocytosis of 137 white blood cells/mL with a 99% lymphocytic predominance, protein of 166 mg/dL, and glucose of 47 mg/dL. MRI of the brain and cervical and thoracic spine with IV gadolinium contrast showed bilateral, bilateral, patchy T2 hyperintensities in the caudate, putamen, and posterior limb of the internal capsule as well as a longitudinally extensive T2-hyperintensity extending from the upper cervical spine to the thoracic spine with associated cord enhancement on postcontrast imaging (figure).

Question for consideration:
1. How does the differential diagnosis change with the laboratory and imaging results?
Figure MRI series of the brain and cervical spine

(A) Fluid-attenuated inversion recovery axial image of the basal ganglia; (B) T2-weighted sagittal MRI series of the cervical spine; (C) corresponding T1-weighted sagittal MRI with gadolinium contrast; and (D) corresponding T2-weighted axial MRI.
Section 3

The neuroimaging suggests that the patient is experiencing a meningoencephalomyelitis, and the CSF profile points to an infectious or inflammatory cause. Flavivirus infection is high on the differential based on the MRI pattern of basal ganglia and thalamic involvement. West Nile virus (due to involvement of the spinal cord), Eastern equine encephalitis (EEE) virus, and California encephalitis virus group (both due to their association with hyponatremia) are all possible pathogens. St. Louis encephalitis, Japanese encephalitis, and tick-borne encephalitis may be more likely to have spinal cord involvement than EEE or California encephalitis. Enteroviruses and Coxackievirus also can cause an encephalitis or myelitis. Mycobacteria and Mycobacterium tuberculosis should be considered due to their predilection for the spinal cord.

Inflammatory disorders such as neuro-Bechet disease also exhibit this radiologic pattern, as well as neoplastic disorders such as primary CNS lymphoma.

Testing for all the considered conditions, including anti-aquaporin-4 antibodies, returned negative. At that point, we decided to treat the patient for an empiric inflammatory meningoencephalomyelitis with a 5-day course of corticosteroids. He responded well to the treatment, regaining almost full strength by the time of his transfer to acute rehabilitation. Plasma exchange was considered after administration of steroids, but given the rapid improvement of symptoms after corticosteroids, it was ultimately deferred.

Several weeks after hospital discharge, CSF testing indicated the presence of glial fibrillary acidic protein (GFAP) antibody, consistent with autoimmune GFAP astrocytopathy. The patient had one flare of his headache that responded to a long-term steroid taper. He has otherwise remained well and has returned to baseline neurologic function and is back to performing his usual activities, including sports.

Discussion

GFAP astrocytopathy is an increasingly recognized form of steroid-responsive autoimmune meningoencephalomyelitis, distinct from infectious and idiopathic meningoencephalomyelitis. A case series examining 102 patients with a confirmed diagnosis shows that the condition typically develops in patients in middle age, with symptoms indicative of meningitis, encephalitis, and myelitis. The most common presenting symptoms are memory loss, headache, blurred vision, seizures, tremor, and mild motor and sensory deficits with a predilection of upper respiratory infection symptoms not uncommonly seen. The timing of the memory loss remains to be defined.

Typical CSF findings show a nonspecific inflammatory pattern of marked pleocytosis (median value of 78/μL) and elevated protein (median 80 mg/dL). GFAP immunoglobulin G present in the CSF appears specific for a meningoencephalitis. However, the antibody has also been shown to be expressed in spinal cord astrocytomas as well as gliomas. One-third of patients with GFAP astrocytopathy had an associated tumor found within 2 years of symptom onset. The most common tumor types include ovarian teratoma, adenocarcinoma (endometrial, esophageal, and renal), and glioma.

Our patient exhibited the most frequent spinal MRI finding of autoimmune GFAP astrocytopathy, a longitudinally extensive T2 hyperintensity. While this can also be indicative of NMO, 2 factors differentiate autoimmune GFAP astrocytopathy from this. Primarily, the spinal cord enhancement appreciated in GFAP is thin, distinctive, and courses along the central canal, corresponding to antigen-enriched regions in rodent spinal cord. This is unlike the hazy parenchymal enhancement of NMO spectrum disorders. While the spinal imaging was consistent with GFAP astrocytopathy, our patient's brain imaging did not reveal the hallmark radial periventricular enhancement appreciated in many patients.

While the condition is noted to be steroid-responsive, there is a tendency for patients to relapse without long-term immunosuppression. Screening for malignancy is also essential, as almost 40% of patients were diagnosed with a neoplasm within 3 months of neurologic onset. Our patient was noted to have a recurrence several months following hospital discharge and placed on a steroid taper. He was screened for malignancy shortly after discharge with no neoplasm found. We plan on repeating this screening every 6 months for up to 2 years.

Prompt clinical suspicion of autoimmune GFAP astrocytopathy and subsequent steroid administration may lead to improved outcomes.

Author contributions

N.M. Patel and J. Bronder: conceptualization, design, and drafting of the manuscript. N. Morris and M. Motta: critical revision of the manuscript.

Study funding

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Disclosure

The authors report no disclosures relevant to the manuscript. Go to Neurology.org/N for full disclosures.

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Mystery Case responses

The Mystery Case series was initiated by the Neurology® Resident & Fellow Section to develop the clinical reasoning skills of trainees. Residency programs, medical student preceptors, and individuals were invited to use this Mystery Case as an educational tool. Responses to multiple choice questions formulated using this case were solicited through a group e-mail sent to the American Academy of Neurology Consortium of Neurology Residents and Fellows and through social media. We received 389 responses. The majority of respondents (72%) had just been in practice for 1–4 years; 57% were residents or fellows while 34% were faculty/board-certified physicians; the remainder were medical students or advanced practice providers. A total of 68% resided outside the United States. A wide range of practice settings was represented.

The 23-year-old patient presented with generalized seizures and a 2-week prodrome of headaches, nausea, confusion, and staring spells. When presented with the pertinent neurologic signs, 27% and 58% correctly localized them to the central spinal cord and CNS above the midpons, respectively. The most common incorrect answer was multifocal meningeal (39%), which although has a role in the differential, is unlikely to cause a CN III lesion with isolated ptosis and therefore is not a preferred response.

When presented with the imaging, 65% correctly identified bilateral, patchy T2 hyperintensities in the caudate, putamen, and posterior limb of the internal capsule in the axial fluid-attenuated inversion recovery sequence and 38% correctly identified a longitudinally extensive hyperintensity extending from the upper cervical spine to the thoracic spine with associated cord enhancement in the T1-weighted sagittal MRI of the cervical spine with gadolinium enhancement. The most frequently selected incorrect answer was a longitudinally extensive cord lesion without enhancement (22%).

Most of the provided diagnostic options were reasonable, reflecting the broad differential diagnosis in this case. The final diagnosis was GFAP astrocytopathy (chosen by 11%), confirmed by the presence of GFAP antibody in the CSF. A longitudinally extensive T2-hyperintense lesion is the most frequent spinal imaging abnormality in this condition; it is characteristically thin and affects the central cord, distinguishing it from the hazy parenchymal enhancement of NMO spectrum disorders.

Nevertheless, NMO (25%) could also explain the patient’s clinical presentation and flavivirus myeloencephalitis (33%) should be high on the list considering the subacute nature of the patient’s symptoms and the basal ganglia and thalamic involvement. ADEM was the most frequently selected response (62%) and, although an appropriate differential, the longitudinally extensive spinal cord lesion (recognized, but less common) and no history of infection or vaccination makes an NMO spectrum disorder the preferred choice of the inflammatory differentials.

This difficult case highlights the need for further awareness of this emerging cause of steroid-responsive autoimmune meningoencephalitis.

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References

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Opinion and Special Articles: Mentoring in neurology
Where are the clinician-scientists? Is residency to blame?

Amr Eliaity, MD, PhD, and Nandakumar S. Narayanan, MD, PhD

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From Alexander Fleming's discovery of penicillin in 1928 to the recent awarding of the 2018 Nobel Prize in Medicine and Physiology to Tasuku Honjo for his work with James Allison on immune checkpoints, physician-scientists have made and continue to make critical contributions to biomedical research. These include internists working in neurosciences such as Roderick MacKinnon, Robert Lefkowitz, and Brian Kobilka who are physician-scientists trained in neurology such as Stanley Prusiner and David Hubel. With only 1.5% of physicians conducting research as their primary profession and competing with a much larger pool of PhDs, a compelling case can be made for why this small pool of physicians must be maintained and expanded.

Much has been written since the last quarter of the 20th century about the demise of the physician-scientist workforce (PSW). The previous NIH Director James Wyngaarden was one of the first to describe this segment as “an endangered species.” That time was the start of a trend in which the proportion of MD applicants for NIH grants has been progressively declining, whereas the corresponding fraction of PhDs increased dramatically (figure, A). In addition, the average age of the PSW is rising (figure, B) because fewer young investigators are entering the pipeline. The PSW advisory committee estimates that approximately 1,000 new physician-scientists need to enter the workforce each year to maintain a steady state. To achieve this goal, reasons for declining interest in academic neurology need to be identified and addressed.

Potential reasons for declining interest in combining neurology and science

From the time of completion of high school, it currently takes 18–24 years to train a laboratory-oriented academic neurologist as opposed to as little as 12 years to become a clinical neurologist. The long training, including 4–6 years of residency and fellowship training with minimal exposure to research, lessens the attractiveness of this career path. Although it could be argued that there is a lot to be learned before embarking on an investigative career, a training requirement spanning 2 decades or more is certainly a deterrent to aspiring neurologists.

With more neurologic knowledge and training requirements for today’s residents, some institutions may hesitate to promote research among residents because of increasing clinical service and limited time for research and/or creativity during residency. Furthermore, residents in more clinically oriented departments may find themselves in an environment with no research mentoring. Little incentive may be available for research-oriented faculty to mentor residents.

Added to the previously mentioned challenges is the mounting educational debt, currently estimated by the Association of American Medical Colleges to average $192,000 for the 2017 class. Medical graduates are meanwhile witnessing the challenges facing their physician-scientist
role models in the current science funding climate together with increasingly onerous research regulations. After all, and as the Deputy Director of the NIH, Michael M. Gottesman has stated, "the best attraction to a clinical research career may be the promise to a physician of committed funding to conduct the clinically oriented or basic research of his or her choice." Together with family considerations and societal pressures toward primary care, today's residents might be under more pressure than ever to find the fastest route to financial stability. Spending an additional 5–10 years in research training to become an independent investigator, while maintaining specialty requirements, does not seem to be a safe career choice for many residents.

**Rescuing the PSW: What can be done during residency?**

The flexibility that characterizes MD-PhD programs and allows integration of clinical and research training has been overlooked in postgraduate training, which is classically divided into long periods of exclusive clinical training devoid of research, especially laboratory-based research. Thus, physician-scientist trainees often spend the years of residency, and often fellowship as well, away from the research world. Re-entry is challenging, with a "holding zone" of variable number of years during which trainees often cannot identify clear milestones, thus the potential for attrition is high.

Federal agencies and institutions that take longer term views of enormous challenges in faculty development may recognize that it is uniquely efficient to invest resources in providing some time, resources, and mentorship to cultivate research during residency. An example effort to bypass the current "linear" model of training is the R25 grant mechanism by the NINDS. Residents in 16 participating neurology departments can apply for support while enrolled in specialized research tracks. These tracks adhere to the principles of Flexible Training in Neurology proposed by the American Neurological Association, with
individuation training that spans the duration of residency. It is important that scientific training should not be made at the expense of rigorous clinical training. Rather, elective time can be organized in a way that allows involvement in research throughout residency. An example timeline is to identify a research mentor in postgraduate year (PGY) 1, 3 months of dedicated research in PGY 2, 4 months in PGY 3, and 4 months in PGY 4. During these research blocks, residents are still expected to continue seeing patients in the continuity-of-care clinic weekly. Residents are encouraged to apply for R25 NIH funding in their PGY 2 or PGY 3 year. Full-time support for research is provided for a minimum of 9 months and a maximum of 12 months during residency. Funded residents can then transition into a research fellowship in their home department or any of the other 15 participating institutions, during which protected research time is supported by R25 funding, with the goal of collecting enough preliminary data to apply for an K award. If successful, awardees will be on a path toward independence by the end of fellowship. We estimate this timeline to save 3–5 years in the transition to independent research careers.

Departments not participating in such NIH funding mechanisms can still apply the same principles. Funding could be obtained from other national organizations and private foundations that have taken interest in the problem such as Howard Hughes Medical Institute, Lasker Foundation, Doris Duke Charitable Foundation, and Burroughs Wellcome Fund. In addition, it should be recognized that teaming up with industry can contribute to scientific training of young investigators, and an increasing number of joint academic–industry fellowship programs have recently been created. This can provide unique perspectives to training in drug discovery and clinical trial methodology, especially considering that one of the major bottlenecks in neurology clinical trials is the limited number of adequately trained neurology trialists. These partnerships can also help young physicians learn how to manage potential conflicts of interest. Internal funding mechanisms exist as well to fund the research training of junior clinicians.

Some programs offer the opportunity to pursue Master’s degree in Science or Clinical Epidemiology, as an additional fully funded year during residency without significant interruption of the resident's clinical experience. Non-degree certificate programs are available as well, whereby dedicated coursework in biostatistics, clinical research, and critical review of the literature is offered. Finally, there are a broad array of mentor-based T32 grants whereby a trainee can dedicate time toward significant research and transition to a clinician-scientist in their future career.

Although these opportunities may be limited by increasing clinical demands, adhering to the principles of flexible training mentioned will likely still be beneficial. For the right trainee, a focused experience may launch a career that helps translate advances from industry to the clinical arena. Although reduction of the time spent in the “holding zone” may contribute to reduced attrition, increasing evidence suggests that mentoring is the single most important contributor to success in transition to independence. In fact, a mentor’s track record often outweighs the mentee’s potential to the point that concerns were raised about a possible demise of meritocracy in NIH funding. This should be taken into consideration when identifying a mentor.

For departments with less research-oriented faculty, mentorship teams could include external members. Speaker series, joint conferences, and networking events that bring together scientists and clinicians who work in close geographical proximity should be organized, and residents should be encouraged to attend. Last but not least, events for residents enrolled in research tracks could be organized at a national level to help exchange of ideas and nurturing a community of shared interests.

Concluding remarks

The quest for advancing the bounds of science is a challenging venture; a sound scientific reasoning cannot always be validated by experimental data, and a highly effective intervention in an animal model often does not translate into a novel therapy for patients. It takes patience and persistence to reach a scientific breakthrough that can alter our understanding/treatment of a disease. This is in contrast to the clinical world where one can quickly experience the gratifying effects of easing someone’s suffering or affecting his/her life. The interface between both worlds is where the role of a physician-scientist lies. He/she is in a unique position to advance medicine both by deriving testable scientific hypotheses from daily clinical observations and by translating laboratory findings into meaningful clinical interventions. Daunting barriers facing aspiring physician-scientists represent the most important threat to the future of academic neurology. For breakthroughs in treatment of neurologic disorders to continue coming about, every effort should be undertaken to save this segment of neurologists.

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Appendix Authors

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Call for Voices: Lived Experiences

The editors of the Neurology specialty site Equity, Diversity, & Inclusion encourage you to submit short first-person accounts (1,000 words or less) of experiences lived within the realm of equity, diversity, and inclusion (EDI) with the goal of informing and enlightening our community on these critical issues. Some topics to consider include, but are not limited to:

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Pearls & Oy-sters

“Pearls and Oy-sters” is a feature focusing on fundamental clinical neurology. Each article addresses a specific niche of neurological disease and provide expertise in the form of clinical insights and tips, i.e., “pearls,” as well as advice for avoiding mistakes, or “oy-sters.” The author may choose to address a particular facet of the approach to neurological disease such as localization, elaboration of a differential diagnosis, evaluation, or treatment. These articles concentrate on what may be found in a textbook and/or provide what textbooks cannot, in the form of knowledge rendered from clinical experience. The target audience consists of those in training; however, the subject matter should be of interest to all in the world of clinical neurology.
Pearls & Oy-ster: Challenging diagnosis of Gerstmann-Sträussler-Scheinker disease

Clinical and imaging findings

Minju Kang, MD, Jeewon Suh, MD, Seong Soo An, PhD, SangYun Kim, MD, PhD, and Young Ho Park, MD, PhD


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Figure Brain MRI and PRNP sequences of the patient and his mother

(A) Axial diffusion-weighted imaging of the patient shows marked high signal intensities in the bilateral cortices, right caudate, and right anterior putamen. (B) Sagittal T1-weighted imaging of the patient shows mild cerebellar atrophy. (C) PRNP sequence of the patient reveals heterozygous substitution from C to T at position 305 of PRNP, resulting in amino acid change from proline to leucine at position 102 (P102L mutation). (D) PRNP sequence of his mother confirms absence of the P102L mutation.

Pearls

- Gerstmann-Sträussler-Scheinker disease (GSS) is a rare prion disease characterized by cerebellar ataxia with progressive cognitive decline.
- GSS is caused by a mutation within the prion protein gene (PRNP), which commonly exhibits an autosomal dominant inheritance pattern. However, a significant portion of previously reported cases show no family history of the disease, and GSS may also occur through de novo mutation of PRNP.

Oy-ster

- GSS is clinically heterogeneous and has no characteristic features on imaging. GSS could be considered in patients experiencing unexplained ataxia and subsequent cognitive decline even in those without a family history of the disease.

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Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.
A 49-year-old man, previously healthy, presented with a 1-year history of progressive gait disturbance, slurred speech, and clumsiness in both hands. He had no history of alcohol or drug abuse. He did not report any family history of neurodegenerative diseases. His 71-year-old mother and 74-year-old father, along with his 3 siblings (2 sisters and 3 brothers), were healthy and neurologically normal. Neurologic examination revealed dysarthria and ataxia. He could not perform tandem gait, and the Romberg test was negative. Motor and sensory functions were normal. Deep tendon reflexes were normal, and there were no pathologic reflexes or abnormal movements. He scored 22 on the Mini-Mental State Examination. Memory and executive function deficits were noted on neuropsychological tests. Routine laboratory tests were normal. There was no evidence for systemic vasculitis, paraneoplastic disorders, or autoimmune thyroiditis. Brain MRI performed 1.3 months after the onset of symptoms showed high signal intensities over the bilateral cortices, right anterior putamen, and right caudate, which were evident on diffusion-weighted imaging (DWI) and fluid attenuated inversion recovery (FLAIR) imaging (figure). Mild cerebellar atrophy was noted on T1-weighted imaging (figure). EEG was normal without periodic synchronous discharges. Routine CSF analysis was unremarkable, but the CSF 14-3-3 protein was positive. Genetic testing showed heterozygous substitution from C to T at position 305 of PRNP, resulting in an amino acid change from proline to leucine at position 102 (P102L mutation) (figure). This confirmed the diagnosis of Gerstmann–Sträussler–Scheinker disease (GSS). Since there was no PRNP mutation in either parent (figure), de novo P102L mutation was suspected in the patient. His motor and verbal abilities rapidly declined. He became akinetic and mute 5 months after the initial visit.

**Discussion**

GSS is a hereditary prion disease characterized by prominent cerebellar ataxia accompanied by gradually progressive cognitive decline. A diagnosis is made by genetic testing to confirm PRNP mutation. Mutations in PRNP often exhibit an autosomal dominant inheritance pattern. However, prior studies including a European cohort study found that one-third of patients with GSS showed no family history of neurodegenerative disease. This was the case in our patient. Although we confirmed P102L mutation in our patient, PRNP mutation was not observed in the patient's parents. In our case, we observed high signal intensities over the bilateral cortices on DWI/FLAIR imaging, which led to further testing for a prior protein-related disease and ultimately the diagnosis of GSS. To our knowledge, there has not been any systematic literature review investigating the family history of GSS and MRI findings.

Here, a systematic literature review was conducted to investigate the clinical manifestation, diagnostic test results, and presence of family history of GSS. Publications listed in PubMed between 2000 and 2017 were searched using the keyword "Gerstmann-Sträussler-Scheinker." Thirty-six case reports (a total of 85 patients) published in English were collected. Clinical presentation and family history of these 85 patients, as well as our patient, are presented in Table e-1 (doi.org/10.5061/dryad.2p66m6nt). Fourteen of 85 cases (16.5%) did not have any family history of GSS. However, it is worth noting that some of these cases had negative family history due to either missing information or early death of first-degree relatives. Among these 14 cases, 6 showed P102L mutation, and the remaining 8 showed different mutations (A133V, D202N, Q217R, P84S, V176G, Six OPRI, Q212P, G131V). Because P102L mutation is known to have high penetrance, incomplete penetrance is likely not the cause of negative family history in the 6 patients with P102L mutation. Interestingly, 2 P102L-mutated patients, including our patient, were confirmed to have de novo mutation of PRNP by sequencing in both parents. However, the mutations exhibited by the remaining 8 patients were not found in patients with GSS with positive family history, suggesting the possibility of incomplete penetrance in these 8 patients. Typically, the genetic prion disease is only considered if the patient has a family history of similar disorders. However, an analysis of literature regarding GSS revealed that a significant proportion of patients with GSS did not have a family history of the disease.

With regard to MRI results, a substantial portion of patients with GSS showed nonspecific findings. Table e-2 (doi.org/10.5061/dryad.2p66m6nt) describes the MRI findings of 63 patients with GSS who underwent brain MRI. Twenty-seven of 63 patients (42.9%) only exhibited either cortical atrophy or cerebellar atrophy. Thirteen patients (20.6%) displayed high signal abnormalities in the cortex, caudate nucleus, or putamen, which were similar to the imaging findings in sporadic Creutzfeldt-Jakob disease.

GSS can manifest various signs and symptoms (Table e-1, doi.org/10.5061/dryad.2p66m6nt). The initial symptoms were reported in 66 patients, of which 15 patients (22.7%) presented with paresthesia or numbness, depression, confusion, and deafness and did not present with ataxia or cerebellar signs at the initial symptoms. Cerebellar dysfunction, however, was observed in all patients at advanced stages of disease. According to our analysis, there seems to be some variability in the initial phenotypic presentation, especially in the early stages of GSS, lacking classical symptoms of other prion protein diseases, like cerebellar dysfunction.

GSS can be challenging to diagnose due to the wide spectrum of clinical phenotypes and imaging findings, as well as ambiguity in family history. Thus, PRNP genetic testing for GSS should be considered in patients with ataxia or cognitive impairment of unknown etiology, even in those without family history.

**Author contributions**

Dr. Kang: study concept and design, acquisition of data, analysis and interpretation. Dr. Suh: acquisition of data. Dr. An: analysis and interpretation. Dr. Kim: critical revision of the
manuscript for important intellectual content. Dr. Park: study concept and design, critical revision of manuscript for important intellectual content, study supervision.

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References

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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: Art and the restoration of identity in dementia

Bryan J. Neth, MD, PhD

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What can we do to restore identity in a disease that strips the very essence of personal identity in nearly every individual unfortunate to meet its path? Willems de Kooning (1904–1997) was one of the most preeminent abstract expressionists of the 20th century. He also was diagnosed with likely mixed dementia after developing significant cognitive and functional impairment beginning in his 70s. Throughout his cognitive decline, de Kooning continued to paint productively at a vigorous rate. The juxtaposition from earlier works is evident in de Kooning’s art after his diagnosis, with increasing simplicity and clean bands of vivid color. Another artist with a known dementia diagnosis is William Utermohlen (1933–2007). After his diagnosis of Alzheimer disease in 1995, he continued to paint self-portraits throughout his cognitive decline. There is a striking contrast of late portraits when compared with prior self-portraits, with an intense fear and yearning to understand his condition. Hauntingly, distinct facial features in his self-portraits are obscured toward the end, as if they have withered into the abyss.

We are fortunate as a society to have had artistic influences like de Kooning and Utermohlen, who have provided us a fundamental glimpse into the mind of dementia. As a neurology resident–physician, I yearn to understand neurologic disease through the lens of patient experience. Indeed, de Kooning’s and Utermohlen’s paintings are several of the best tools we currently have to understand the perspective of dementia.

Alzheimer disease and the other dementias characteristically lead to a progressive decline in cognition, functional status, and behavior. The memories that strengthen our connections throughout life are ultimately slashed until the only remaining memories are distant recollections from childhood. These are truly some of the saddest diagnoses in all of medicine as the resultant depersonalization steals patients of their lifelong identity.

I have experienced the great gift that art may provide individuals with cognitive impairment. The empowerment and pride that shines from faces of those who have created a painting or written a haiku for the first time is unforgettable. In the following paragraphs, I describe my participation with an arts-based dementia support group and argue that engagement in the arts should be a pillar for the current palliative management of dementia.

In early 2012, I had the opportunity to work with a multidisciplinary team of fellow medical students, geriatricians, and other providers to develop a cognitive support group for individuals with all forms of mild cognitive impairment and dementia. Group participants were community-dwelling adults who varied significantly throughout the spectrum of dementia. Participants included a former aerospace engineer who was functioning independently with no overt signs of cognitive impairment, a former high school teacher and avid landscape painter who needed help with activities of daily living (ADLs)/instrumental activities of daily living (IADLs), and participants with obvious functional decline who necessitated prompting for verbal communication and were dependent in nearly all ADLs/IADLs.

From the Department of Neurology, Mayo Clinic, Rochester, MN.
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Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the author, if any, are provided at the end of the article.
Our primary outcome measure at group onset was change in Montreal Cognitive Assessment (MoCA). While we realized the likelihood of substantial cognitive improvement was negligible in those with established diagnoses, we searched for an objective measure to quantify group effect. Our groups were designed to run in parallel with a social support group for caregivers. Groups lasted 10 weeks, with monthly maintenance groups for participants who had previously participated in our 10-week sessions.

The initial design of our Brain Fitness group was to focus on classic cognitively enhancing activities. These included tasks that stressed memory performance, attention, and visuospatial skills. After about 2 sessions of co-leading groups it became apparent that traditional cognitively focused activities were poorly fitted for our intended group participants. The frustration and anguish was palpable. I distinctly remember the minutes of silence waiting for group members to answer memory challenge questions or recalling the face of a commonly known 1950s celebrity. I felt horrible. My group co-leader, Gerard, and I wanted to positively affect group participants. We were eager incoming second-year medical students. However, we could not overcome the feeling that providing another source of stress in our group participants was not our ultimate mission—despite our objective goal of cognitive improvement. We had one saving grace...the Ball Game.

When Gerard and I were planning our first group, we added one pure fun activity at the end of each session. This activity for the first week was the Ball Game, which consisted of rolling a tennis ball on a flat boardroom table randomly to group participants. It was groundbreaking for us. Participants loved it, after what seemed like a grueling 60–75 minutes of memory activities. We had the capability to make the game more challenging by adding 2, 3, and 4 balls at a time—or by bouncing the tennis balls instead of rolling them. When we added music from the 1940–1950s, energy flowed through the room like electricity through standing water. Participants who had previously remained mute and emotionless throughout much of the group activities began to dance to the music and fight for incoming balls. It became apparent that we needed to continue with the Ball Game. Activities were planned for each week in advance, but after its resounding success, we incorporated it weekly.

Throughout the first group, we learned that our more intensive cognitive-based activities and memory challenges were a source of profound frustration with participants. MoCA scores were not significantly different pre-vs-post group. With our current state of tools, altering cognitive endpoints with brain training activities after diagnosis of mild cognitive impairment is a Herculean effort. Given the success of our more creative activities, we reconvened with our mentors and switched to a fully arts-based curriculum for our second 10-week group.

The second rendition of the Brain Fitness group consisted of one longitudinal project supplemented by a weekly curriculum. Our first longitudinal project was a combined group painting. We decided to dedicate one color to each week. The first several weeks were challenging. We had 1–2 group members who actively participated while the remaining added very few brush strokes to the final canvas. The early adopters were artists themselves or artistically inclined. Yet, with the persistent motivation and encouragement by active participants, we were able to engage every member of the group. Several 80-year-olds from Appalachia who had never picked up a paintbrush in their lives actively participated in them-altering contributions to the group artwork. The most exciting part of this process was seeing the more artistically experienced group members teaching other participants how to paint. This was all we truly desired to achieve—to facilitate interaction between individuals with similar life experiences, who have largely been isolated from social engagement. We achieved this goal. A satisfaction survey at the end of our first arts-based group resulted in rankings of average overall group satisfaction, enjoyment of arts-based activities, and weekly group painting as "excellent" on a scale of excellent–good–average–poor. All participants would have recommended the group to others.

Our next longitudinal project incorporated several creative tasks. First, we spent 2 weeks teaching participants about photography and specific features in a photograph that makes it appealing. Afterwards, cameras were supplied to group participants with the goal of capturing photographs throughout their daily lives over a week. When participants returned with their photographs, we went through each as a group. Then, participants decided on which of the photographs they would like to print. We eventually painted frames to hold the photographs and wrote a haiku about each photograph with presentation of this project in front of families and friends at group conclusion.

Throughout the 5 years I helped facilitate the Brain Fitness group, I witnessed the personal, social, and skill-building transformation that group participants made. Subjectively, one group participant described our group as "A place where I don’t have to be perfect." Other feedback included, "My experience makes me want to do more activities at home," and "I made new friends that have the same interests." Despite these encouraging reflections, the clinical decline became evident. Even our most high-functioning participants began to progress in their clinical course. Over months to years in our maintenance groups, several participants returned to group with less vigor and poorer recollection of other group members and our previous group activities.

While we currently lack a disease-modifying therapeutic for Alzheimer disease and related disorders, there is hope to help restore identity throughout the progression of dementia. I strongly encourage every medical student, resident, attending
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Teaching NeuroImages: Neurolymphomatosis

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A 64-year-old woman with a history of diffuse large B-cell lymphoma presented with 3 months of progressive pain and weakness. Examination was notable for asymmetric face, arm, and leg weakness with absent reflexes. CSF was normal twice, including cytology and flow cytometry. PET showed widespread avidity (figure 1), including the bilateral brachial and lumbosacral plexi. Nerve conduction study/EMG showed reduced motor amplitudes but normal sensory responses, indicating that Wallerian degeneration had not yet progressed distal to the dorsal root ganglia—underscoring the urgency of timely diagnosis and treatment. Sciatic nerve biopsy confirmed neurolymphomatosis (figure 2). She received 2 cycles of rituximab plus ifosfamide, carboplatin, and etoposide chemotherapy with resolution of PET avidity, followed by autologous bone marrow transplant. Neurolymphomatosis is characterized by malignant invasion of nerves, often presenting with severe, asymmetric pain. CSF studies have low sensitivity; thus, diagnosis often depends on PET and biopsy. Symptoms and imaging abnormalities often resolve with systemic chemotherapy; however, relapse is common—with 1 large case series showing a median survival of 10 months and 24% survival at 36 months.

Figure 1 PET showed widespread fluorodeoxyglucose avidity (A), including right facial nerve (B), sciatic and femoral nerves (C), bilateral brachial and lumbosacral plexi (D), and C3/C4 roots (E), with resolution of PET avidity after chemotherapy (F)

Author contributions
S.R. DeBoer and S. Lesche: drafting/revising the manuscript, data acquisition, study concept or design, analysis or interpretation of data, accepts responsibility for conduct of research, and will give final approval. F. J. Rodriguez: data acquisition, analysis or interpretation of data, accepts

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Figure 2 Sciatic nerve fascicle biopsy (400×)

H&E (A) shows infiltration and disruption by malignant cells. Anti-CD20 immunostain (B) demonstrating large neoplastic B cells, in a background of reactive CD3+ T cells (not shown).

Responsibility for conduct of research, and will give final approval. L. W. Ostrow: drafting/revising the manuscript, data acquisition, study concept or design, analysis or interpretation of data, accepts responsibility for conduct of research and will give final approval, acquisition of data, and study supervision.

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References
Teaching NeuroImages: Advanced imaging of neurosarcoidosis with $^{68}$Ga-DOTATATE PET/CT

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Figure $^{68}$Ga-DOTATATE PET/CT, MRI, and histology

A 45-year-old man presented with increasing visual impairment. MRI showed a nonspecific lesion at the cavernous sinus; an additional $^{68}$Ga-DOTATATE PET/CT showed an extraordinarily high $^{68}$Ga-DOTATATE uptake of the lesion (figure). Stereotactic brain biopsy was performed and revealed an initial manifestation of neurosarcoidosis. $^{68}$Ga-DOTATATE targets the somatostatin receptor (SSR), which is expressed by tumor cells in malignancies such as neuroendocrine tumors and meningioma, but also by activated macrophages, as present in neurosarcoidosis. Targeted radionuclide therapies using SSR ligands labeled with beta-emitting isotopes might offer additional therapeutic options in patients with treatment-refractory neurosarcoidosis, as also effectively applied in SSR-positive malignancies.

Author contributions
Dr. Unterrainer: study design, data collection, drafting and revising the manuscript. Dr. Ruf: acquisition and analysis of histopathology, revision of manuscript. Dr. Ilhan: analysis of PET/CT scan, revision of manuscript. Dr. Vetterman: analysis of PET/CT scan, revision of

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manuscript. Dr. Holzgreve: study design, data collection, revision of manuscript. Dr. Cyran: analysis of PET/CT and MRI scans, revision of manuscript. Dr. Tonon: data collection, revision of manuscript. Dr. Bartenstein: study supervision and analysis of PET scans, revision of manuscript. Dr. Albert: study design, data collection, drafting and revision of manuscript.

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