TEXAS NEUROLOGICAL SOCIETY WINTER 2025

Broca's Area

The Voice of Texas Neurology

President's Message

Michael Soileau, MD, FAAN
TNS President

The new year is upon us! As I reflect on 2024, it has been a truly amazing year that seems to have flown by in a mere blink of the eye! TNS and its committees have been hard at work relentlessly pursuing the core values of our organizations' founders (as mentioned in the summer 2024 Broca's Area).

Thanks to the leadership of Drs. Sara Austin (Austin, TX) and Kim Monday (Houston, TX), the legislative committee has been extremely active hitting the ground running.

Recently, the committee orchestrated a wonderful "show and tell" as well as an informational session to the State of Texas legislators and staff on the importance and value of obtaining funding for mobile stroke units in order to reduce the time to receive excellent care and increase the efficiency of stroke treatment around the state. In addition, the State of Texas Lieutenant Governor has asked our organization to help spearhead and shape the "Dementia Prevention Research Institute of Texas" that was recently announced. We are excited to be part of a state that is tackling an ubiquitous disease such as dementia head on.

The medical economics committee (under the direction of Dr. Eddie Patton (Houston, TX)) has been working hard to provide TNS updates with regard to advocacy and legislation changes by ensuring there is a succinct source of information provided, either through handouts or video series. Healthcare is moving at a rapid pace and constantly changing. Therefore, we need to ensure our members have this information at their fingertips. I am grateful for the AAN for putting together such a wonderful and robust monthly legislative newsletter that accomplishes just that. In addition, the committee has worked to provide a handout that can be placed in waiting rooms for patients and their loved ones with a very simple to read explanation of select 2025 changes to Medicare, such as the elimination of the donut hole, limiting out of pocket costs to $2000 and to process "opt-in."

The resident committee, at the direction of Dr. Yessar Hussain (Austin, TX) has expanded to include more trainees such as medical students. In addition, there is now an additional membership subtype for trainees so they can start learning, networking, and advocating early in their journey to become a neurologist! The meetings have been positive and encouraging to listen to both residents, program directors, and medical students engage and network with the ideas of how to better support, learn from, and encourage the future of neurology.

In addition, we now have a newly-formed independent practice committee led by Dr. Bill Gilmer (Houston, TX) to brainstorm on ways that we can address challenges for independent practices not only at the state level but also at the national level.

I have also asked for an ad hoc committee of advanced practice practitioners (APPs) (led by Co-chairs Meredith Hatcher, PA-C and Karina Patel, PA-C both of Georgetown, TX) to being meeting and brainstorming on ways in which TNS can further support, educate, and collaborate with these extremely valuable members of our healthcare team. The several meetings that I have had the privilege of attending have been delightful and were filled with robust discussion on ideas moving forward. For example, there is now a dedicated place on the webpage where APPs can go for information (a work in progress) as well as collaboration with the education committee on how we can provide specific educational content that APPs would see as valuable. These ideas and content are already in the works!

At the direction of Dr. Katie Hendley (Lubbock, TX), our membership committee continues to work on ways in which we can promote our historical organization to those in our state and beyond. Doing so opens up our value to more and more members including neurology trainees as mentioned previously.

The communications committee headed by Dr. Shivika Chandra (Houston, TX) is continuing to collaborate with our social media team to efficiently disseminate the wonderful work our organization is performing.

Our grants committee led by Dr. Waleed El-Feky (Dallas, TX) continues to receive more and more applications for simply outstanding and exceptional research, ideas, and scholarly activity! It has been a pure joy to see this program expand so rapidly and swiftly all with the idea to improve neurological care around the state.

Last and certainly not least, our education committee led by Dr. Erin Furr-Stimming (Houston, TX) has worked closely with our program directors for both the winter and the summer conferences to continue building an enlightening and valuable program for us.

As you can see, there has been a lot going on within the organization, and we hope that you look forward as much as I do to see the fruit of this labor. I am wishing you a pleasant start to a successful new year!

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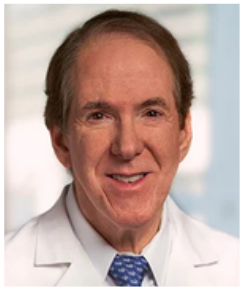

Editor's Notes

Randolph W. Evans, MD

THIS ISSUE

I thank our officers and other contributors for their excellent submissions to this issue. We look forward to seeing you at the TNS Winter Conference at the Hyatt Regency in Austin. Program directors Sujani Bandela and Mirla Avila; Erin Furr-Stimming, chair; and the education committee have planned an excellent program.

GRACE SLICK AND WHITE RABBIT: ONE PILL MAKES YOU LARGER. PSYCHEDELIC ROCK

Grace Slick (1939-) wrote "White Rabbit" in 1966 on her $80 piano with missing keys[1,2] "With lyrics based on 'Alice's Adventures in Wonderland,' it became a touchstone of psychedelic rock." After taking LSD in 1963, Slick listened to a bolero about 50 times which inspired the music.

The song was released by Jefferson Airplane in 1967 on its "Surrealistic Pillow" album and as a single (peaked at number 8 on the pop chart). The song immediately became part of the soundtrack for the Summer of Love.

"One pill makes you larger
And one pill makes you small
And the ones that mother gives you
Don't do anything at all
Go ask Alice
When she's ten feet tall
And if you go chasing rabbits
And you know you're going to fall
Tell 'em a hookah-smoking caterpillar
Has given you the call
Call Alice
When she was just small
When the men on the chessboard
Get up and tell you where to go
And you've just had some kind of mushroom
And your mind is moving low
Go ask Alice
I think she'll know
When logic and proportion
Have fallen sloppy dead
And the White Knight is talking backwards
And the Red Queen's off with her head
Remember what the dormouse said
Feed your head
Feed your head"

Slick stated in 2016, "To this day, I don't think most people realize the song was aimed at parents who drank and told their kids not to do drugs. I felt they were full of crap, but to write a good song, you need a few more words than that."[1]

Notable performances include the following: 1969 Woodstock;[3] "White Rabbit" and "Somebody to Love" on Dick Clark's "American Bandstand" in 1967 including the interview with the band;[4] and the isolated track of her vocals [5].

In a 1998 VH1 Interview, Slick stated, "All rock-and-rollers over the age of 50 look stupid and should retire." In a 2007 interview, she stated, "You can do jazz, classical, blues, opera, country until you're 150, but rap and rock and roll are really a way for young people to get their anger out." The Rolling Stones don't agree.

PSYCHEDELICS FOR THE TREATMENT OF HEADACHES

In 1938, the Swiss chemist, Albert Hofman, synthesized lysergic acid diethylamide (LSD) as a possible respiratory and circulatory stimulant. In 1943, Hofman accidently ingested LSD and discovered the hallucinogenic effect.[6] Three days later, he took an intentional dose and had an incredible bicycle ride on his way home from the lab (April 19, "bicycle day").

The term psychedelic (from Greek for mind manifesting) was coined by psychiatrist Humphry Osmond, in 1956, first introduced at the 1957 meeting of the New York Academy of Sciences, and published in their "Annals."[7,8] LSD was classified as a Schedule 1 drug in 1968.

In 1953, Osmond supervised Aldous Huxley's experience with mescaline. Huxley later wrote, "The Doors of Perception" based on his experience.[9] His book editor said, "You are the most articulate guinea pig that any scientist could hope to engage."

Alice stretched tall (illustration by Sir John Tenniel, 1865)

Mescaline (found in the peyote cactus), psilocybin (found in Psilocybe or "magic" mushrooms or "shrooms"), and lysergic acid diethylamide (LSD) are 5-hydroxytryptamine (5-HT)2A receptor agonists which produce similar altered states of consciousness.[10] Methysergide, a semsynthetic ergot alkaloid derived from LSD, was first tested as a migraine preventive agent in 1959.[11] Ergotamine and dihydroergotamine are chemically related.[12] Psilocybin might be effective for migraine and cluster headache prevention.[13] Low dose oral psilocybin (psychedelic mushrooms) and LSD may be effective for prevention and acute treatment.[14] Many of you are familiar with Clusterbusters.[15]

ALICE IN WONDERLAND SYNDROME (AIWS)

In 1955, Todd named this syndrome in describing "a singular group of symptoms intimately associated with migraine and epilepsy"[16] after the book, "Alice's Adventures in Wonderland," which was published in 1864 by Charles Lutwidge Dodgson under

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the pseudonym of Lewis Carroll (the Latinization of Lutwidge Charles). Dodgson was a Professor of Mathematics at Oxford University and a migraineur. There is speculation that he might have had the syndrome.[17] Spierer speculates that Dodgson may have had temporal lobe epilepsy.[18]

In the first chapter of the book, Alice jumps down a rabbit hole and lands in a hallway where she finds a bottle, which she drinks from, causing her to shrink: "I must be shutting up like a telescope.' And so it was indeed: she was now only 10 inches high..." Later, she eats a piece of cake that makes her grow (figure): "Curiouser and couriouser!' cried Alice...; 'now I'm opening out like the largest telescope that ever was! Good-bye, feet!' (for when she looked down at her feet, they seemed to be almost out of sight, they were getting so far off.)" The White Rabbit was also introduced in the first chapter.

The first description by Lippman was in 1952 when he reported 7 patients with migraines associated with unusual distortions of body image:[19] "Occasionally the patient has an attack where she feels small, about 1 foot high." Another patient had the sensation of her "left ear ballooning out six inches or more." A third patient described his sensations: "the body is as if someone had drawn a vertical line separating the two halves. The right half seems to be twice the size of the left half." And a fourth noted, "I feel that my body is growing larger and larger until is seems to occupy the whole room."

AIWS is a rare perceptual disorder of impaired visual perception or metamorphopsias, abnormal body schema, and distorted experience of time.[20],[21],[22] About 170 cases have been reported. However, AIWS may not be that rare. In a cross-sectional study of 297 people with a median age of 25.7 years, the lifetime prevalence of various perceptions was as follows: teleopsia, 30.3%; dysmorphopsia, 18.5%; macropsia, 15.1%; and micropsia, 14.1%.[23]

AIWS can occur at any age but is more common in children and adolescents. Causes include migraine, viral encephalitis, epilepsy, Epstein-Barr virus, COVID-2, other infections, head trauma, stroke, substance induced, topiramate,[24] and idiopathic.[25] Many of the rare cases where lesions have been identified are localized to the right occipitoparietal lobe.[26] In a retrospective study of 37 cases of lesion-induced AIWS, "...>85% demonstrated shared connectivity to the right extrastriate body area, known to be selectively activated by viewing body part images, and the inferior parietal cortex, involved in size and scale judgements. This pattern was uniquely characteristic of AIWS when compared with other neuropsychiatric disorders."[27]

Visual hallucinations, distortions, and illusions that are reported in migraine include the following: zoopsia (visual hallucinations containing complex objects, such as people and animals); achromatopsia (no perception of color); prosopagnosia (inability to recognize faces); visual agnosia (inability to recognize objects); akinetopsia (loss of ability to perceive visual motion); metamorphopsia (distortion of the shapes of objects); micropsia (objects appear too small); macropsia (objects appear too large); teleopsia (objects seem far away); pelopsia (things are larger than they are because they appear to be closer); lilliputianism (people appear too small); multiple images; persistent positive visual phenomena (diffuse small particles, such as TV static or dots, in the entire visual field lasting months to years); palinopsia (the persistence or recurrence of visual images after the exciting stimulus object is removed); cerebral polyopia (the perception of multiple images); and tilted and upside-down vision.[28]

In a pediatric study of 48 patients,[29] visual symptoms included micropsia (69%), teleopsia (50%), macropsia (25%), metamorphopsia (15%), and pelopsia (10%). Etiologies included infection in 33%, migraine in 6%, and trauma in 6%.

In a prospective study at an adult headache center,[30] 16% reported a history of AIWS including the following: micro- and/or telopsia in 72.9%, micro- and/or macrosomatognosia in 49.6% and macro- and/or pelopsia in 38.3% with an average duration of half an hour. AIWS symptoms occurred in association with headache in 65.1% and 53.7% had their first episode at the age of 18 years or earlier.

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Advocacy Update

Kimberly Monday, MD, Legislative Affairs Chair and Tom Holloway, TNS Lead Lobbyist

Funding and Support for Mobile Stroke Units

As we prepare for the 89th Legislative Session, the Texas Neurological Society continues its advocacy to restore and expand funding to support Mobile Stroke Units (MSUs) in Texas.

Mobile Stroke Units (MSUs) are specialized ambulances equipped with a CT scanner and staff by neurologist-led medical teams trained to diagnose and treat stroke patients on-site. This novel approach to stroke care drastically reduces the time to initial intervention, improving survival rates and reducing long-term stroke-related disability. [1],[2],[3]

In 2019, the Texas legislature demonstrated its commitment to mobile stroke care by appropriating $1 million to support MSU operations in Texas. This year, TNS is lobbing for additional grant funding for new MSUs across the state as well as regulatory strategies that allow MSUs to bill for the performance of diagnostic, therapeutic and transport services.

Over the past year, the TNS lobby team has actively worked to educate and engage lawmakers about the benefits of MSUs. Jim Grotta, M.D. and his team have been vital to providing clear statistics supporting the financial benefit MSUs provide to the State of Texas.

In October, TNS hosted an ice cream social near the Texas Capitol to give legislative staff the opportunity to see an MSU up close and hear directly from TNS's own James Grotta, MD, about the potential MSUs have to revolutionize stroke care in Texas. In addition, the TNS lobby team has also held a series of productive meetings with House Appropriations Chairman Greg Bonnen, MD (R-Galveston), a neurosurgeon, regarding the need to restore funding to the MSU grant program and other policy changes that could support the operation and expansion of MSUs across the state.

The Texas Neurological Society will continue to work with legislators to prioritize funding for MSUs and help establish Texas as a national leader in advanced stroke care.

Dementia Prevention and Research Institute of Texas (DPRIT)

Last month, Lt. Governor Dan Patrick announced Dementia Prevention Research Institute of Texas (DPRIT) as a major legislative priority this session. The creation of the DPRIT would be a groundbreaking research initiative designed to position Texas as a national leader in dementia care and neurodegenerative research.

Modeled after the successful Cancer Prevention Research Institute of Texas (CPRIT), this program is intended to provide state-supported funding to support cutting-edge medical research into the prevention, diagnosis, and treatment of diseases such as Alzheimer's, Parkinson's, frontotemporal dementia, and other cognitive impairments.

According to Lt. Governor Dan Patrick, the DPRIT initiative will support innovative research at some of Texas' premier medical research institution, accelerate scientific discoveries, and improve care delivery for millions of Texans living with these disorders.

To help support the DPRIT initiative, the Texas Neurological Society has assembled an advisory group of leading neurologists specializing in Alzheimer's and dementia care to help advise Lt. Gov. Patrick and others.

- Sara Austin, M.D. (Austin)
- John Bertelson, M.D. (Austin)
- Branden Kelly, M.D. (Dallas)
- Joseph C. Masdeu, M.D., Ph.D. (Houston)
- Kim Monday, M.D. (Houston), *TNS Legislative Affairs Chair*
- Alicia Parker, M.D. (San Antonio)
- Paul E. Schulz, M.D. (Houston)
- Michael Soileau, M.D. (Georgetown)
- Melissa M. Yu, M.D. (Houston)

These experts will help provide insight into the program structure, identify promising research initiative, offer supportive testimony during the legislative process, and answer technical or medical questions regarding the specific neurodegenerative conditions one would expect to see included in DPRIT.

This session, the Texas Neurological Society is fully committed to supporting the DPRIT initiative and we expect to continue working closely with legislators in the months ahead to see it signed into law.

Texas Neurology Day at the Capitol: April 8, 2024

On Tuesday, April 8, please join us for Texas Neurology Day at the State Capitol in Austin!

As in previous legislative sessions, TNS' official advocacy day will be held in conjunction with the Texas Medical Association's "First Tuesday" event (please wear your white coat!) and will give participating neurologists a unique opportunity to meet with lawmakers face-to-face and discuss the policy issues that matter most to your practice and your patients.

No policy expertise is necessary to participate. The TNS lobby team will provide talking points and background information on our full legislative agenda, which includes mobile stroke units, DPRIT, medical cannabis, prior authorization, and other identified priorities.

For more details or to sign up for TNS Legislative Advocacy Day, please contact TNS Executive Director Ky Camero at ky@cameroams.com. We'll see you in Austin!

Mobile Stroke Units: Beyond Thrombolysis

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TNS LOBBY DAY
April 1, 2025

More Information Coming Soon!

ONLINE REGISTRATION AVAILABLE UNTIL JANUARY 24TH

REGISTER NOW!

Calling All Neurology APPs!

We now have our APP committee up and running! We are working hard to create a home for Texas Neurology APPs including CME content for future TNS conferences, social events, networking, and more. At the winter TNS conference, please join us for one or both of our get togethers: Friday APP meet up during the conference lunch break and/or Happy Hour Saturday evening following the conclusion of that day's conference content.

Please see the meeting app or schedule for more details to come.

Hope to see you all soon!

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Resident Housing *stipend*

The TNS offers a housing stipend to all residents who attend the meeting. Each resident who applies for the stipend will be presented with a housing stipend reimbursement from upon check-in. This form should be filled out and returned to the TNS registration table or business office within a week of the meeting. Each resident will have one night reimbursed in host hotel or an equivalent hotel, tax, and self-parking.

Resident Lunch and Symposium

The TNS is hosting a Resident Luncheon and Symposium on Saturday, February 1st. All residents attending the conference are strongly encouraged to attend. Please RSVP on your Registration Form.

Resident Luncheon & Symposium Topics:

- Financial Planning 101 with Eric Anderson, CPA
- Contracts - What you need to know with Michael Stern, JD
- Business of Neurology Rotation - Have you Heard About It?

Resident Poster Competition

The TNS will be hosting a resident poster competition this year:

- **Poster Presentation and Viewing**
  Friday, January 31st during the welcome reception
- **Poster Judging**
  Saturday, February 1st starting at 8:00 am
- **Poster Presentation of Winners Announcement**
  Saturday, February 1st after the final break of the day

Applications and Guidelines can be found on the TNS website.

Prizes

1st place - $1,000
2nd place - $500
3rd place - $250

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On the Comprehensive Neurology Subspeciality - is it time for the Fellowship? A Review and Summary of Selected: Literature

Lawrence Buxton, MD, PhD, FAAN

In the past three decades, the field of Neurology has made significant gains in the diagnosis and treatment of neurologic disease. Effective treats are now available for diseases such as multiple sclerosis, myasthenia gravis, spinal muscular atrophy, couple with more accurate diagnostic testing for these disorders. Moreover, in the same time frame, new neurologic fellowship (post residency) programs are now offered in the areas of stroke, neuro-critical care, sports neurology and neuro-palliative care. However, at the same time, there has been a troubling concern about the current perceived value and effectiveness of the general neurology residency program, now preferably called the comprehensive neurology residency.

Historical Perspective

The purpose of this paper is to outline and describe current challenges facing the comprehensive neurology residency, in a historical context, and then pose the purpose and benefits of a Fellowship for post comprehensive neurology residency physicians.

In the article, "Is General Neurology a Dying Specialty?" (Neurology Today, February, 2020) Orly Avitzur, MD, Past President of the American Academy of Neurology (AAN) related that the percentage of neurologists who described themselves as general neurologists was 40.1 percent in 2015 while only 33 percent did so in 2019. The drift toward specialization was further described showing that a 2019 AAN Membership Insights report revealed the median age of general neurologists was 56, whereas the median age of specialists in movement disorders was 47, epilepsy and vascular neurology 46 and sports neurology 39. A paper in Neurology in 2017, by Abhimanyu Mahajan, MD reported that 90 percent of respondents pursued a fellowship for sub-specialty after general neurology residency. There is no reason to suspect the percentage for fellowship applicants has decreased. Academic neurology leaders realized there was a perfect storm occurring in the specialty, with the aging of the national population, in combination with the retirement of neurologists and the increased need for neurologic services by the patient population.

There are multiple reasons why fewer neurology residents choose comprehensive neurology as a sub specialty. Louise Klebanoff, MD, chief of general neurology for the Department of Neurology at Weill Cornell Medical College feels that the value of comprehensive neurology is not emphasized to neurology residents. While there is a clear need for comprehensive neurologists in academic medical centers and in the private sector, there is a significant shortage of comprehensive neurologists. Dr. Klebanoff reports that at Cornell, with a neurology staff of 60, there are only five comprehensive neurologists. While it is clear that general neurology is needed to effectively run academic neurology programs, Dr. Klebanoff further comments "Accordingly, we are regarded as the lower tier of everything: salary, recognition, and promotion," There is a perception that it is difficult for academic comprehensive neurologists to prove excellence in regional or national reputation in the current academic setting This affects academic promotions as well as fiscal considerations.

With similar numbers, Bruce R. Kastin, MD, Chief of the division of comprehensive neurology and the outpatient medical director for Neurology at Massachusetts General Hospital (MGH) reports that there were only 6 General neurologists at the MGH with a Department of 120 faculty members AT MGH, in trying to counter the perception of decreased value and challenges for promotion, Dr. Kastin has created a clinician-educator promotion track for comprehensive neurologist who are committed to both patient care and medical education.

In the article, "How Advanced Training Programs Pave A Way Forward for General Neurology" (Neurology Today, July, 2023" Jessica Kraker, MD, FAAN, a neurology residency program director and Assistant Professor of neurology at Tulane University opines "For whatever reason, becoming a general neurologist is not often seen to be as prestigious as becoming a subspecialist," "She believes there has to be framing of general neurology as an esteemed, rewarding career and supported by academia. Over the past 4 decades there has been a fundamental change in the purpose of the neurology residency. In the 1970s and 1980s, those who completed a general neurology residency were generally able to enter private practice and direct patient care and competently perform ancillary services such as reading EEG and performing electrodiagnostic evaluations ie EMG, NCV. At the present time, neurology residents don't give much credence to entering neurology workforce following completion of their residency, as evidenced by the large number of them choosing subspecialities.

In current general neurology residency programs, in the opinion of the author, one major goal of the neurology residency is to prepare residents for a fellowship. Supporting this observation is the amount of time residents spent in second and third year choosing and selecting their fellowships In the opinion of the author, very few graduating neurology residents see themselves able to directly enter private practice or general neurology practice. The majority of their patient exposure in the residency program is in the inpatient area-they are not adequately prepared for outpatient neurology. Dr. Kraker believes that the resident continuity clinic is probably the only exposure the resident has to general neurology and that, by itself, is not a true or valid representation of a fulfilling career offered by comprehensive neurology.

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Continued...

The Fellowship

With increasing neurology subspecialization, there is still a palpable demonstrable need for comprehensive neurology training. According to Jessamyn Conell-Price, MD, MS, director of the University of California, San Francisco (UCSF) general neurology fellowship at the UCSF Weill Institute for Neurosciences, there are some clinical and diagnostic challenges that do not fit neatly into a particular subspecialty and it is this type of clinical case where more experience would be invaluable to a comprehensive neurologist in neurology practice.

Several academic centers are now providing one year fellowship programs to improve clinical practice as well as providing opportunities for research, public health initiatives and community engagement. Stanford, University of California, San Francisco (UCSF), and Mass General (MGH) are currently offering fellowship positions and have different methods in offering the fellowships.

The UCSF program focuses on clinical care for developmental syndromes, neurologic complications of systemic disease, and evaluation of complicated neurologic clinical and diagnostic cases. The Fellows spend half of their time in a general outpatient practice, a quarter of their time devoted to clinical work or specific rotations, and the remaining quarter of time dedicated to research, public health, or clinical practice improvement.

At the same time, the Fellows can choose an individual track for their program: novel clinical pathways, education and training, or community engagement.

The fellowship program at Mass General (MGH) was initially started by Nagagopal Venna, MD who began the program in 2007 and was interested in complicated neurologic disorders - he called these cases "mysteriomas". He was very interested in autoimmune neurology and neuinfectious diseases after his work with HIV at Boston City Hospital in the 1980s. The program is now directed by Haatem Reda, MD.

In 2017, the fellowship changed its name from fellowship in "advanced general neurology" to "advanced general and autoimmune neurology (AGAIN). The Fellows gain considerable experience in managing immunomodulatory regimens and rotate through multiple clinics including rheumatology, infectious disease and subspecialty areas in neurology. Over the past 5 years, the number of applicants a year has grown from four to five a year to thirty.

The Stanford University program is referred to as a comprehensive neurology instructorship program and recognizes that only 24 percent of neurology residents are interested in career comprehensive neurology. The program has the flexibility for participants to pursue sub specialties they may have no experienced during their residencies due to inpatient obligations and to gain further experience in taking care of common neurologic disorders. They are also provided the opportunity to rotate through other specialties such as neurosurgery, sleep medicine, physiatry and rheumatology.

Reimbursement is the challenge for the fellowship program. Following the internal medicine model for post residency training, the fellow could serve as Faculty for a continuity clinic as part of his fellowship and bill for services or in some fashion bill patients directly (?) There has not been much written on reimbursement for the fellowship. In the Stanford program, the fellow serves in some fashion as an instructor although it is not clear how funding plays a role.

There are no subspecialty boards for the comprehensive neurology fellowship. Thus far, the fellowship programs are apparently tailored to the academic and professional needs of the fellow. The goal, however, is for the fellow to practice comprehensive neurology when completing the program.

In summary, it is the opinion of the author of this article that a fellowship in comprehensive neurology is one viable consideration to resolve the significant shortage of comprehensive neurologists currently existing in the nation. Neurology has been the recipient of the perfect storm, the aging of the country's population with increasing need for neurology services, the ever present shortage of those services secondary to multiple factors - the Covid-19 pandemic, the aging of the neurology physician supply coupled with neurology residents choosing fellowship training thus postponing their entry into the workforce. It is clear that the current neurology residency curriculum is not producing sufficient numbers of comprehensive neurologists and it will be a long time before changes in the basic neurology residency are made. It is incumbent upon leading academic neurology training programs to insure the integrity - and effectiveness of comprehensive neurology. This will require novel thinking and creative changes in uncharted academic territory.

In the words of Southern humorist Lewis Grizzard, "Life is like a dogsled team. If you ain't the lead dog, the scenery never changes."

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A Deeper Dive into Steroid Dementia Syndrome

Grace Cardenas, Medical Student, Baylor College of Medicine

A 34-year-old female presenting to the hospital with one month of back pain and progressive generalized weakness requiring assistance to ambulate. According to her husband, she also had worsening short-term memory loss, tremulous-ness, and excessive anxiety. She was uncertain of many aspects of her recent medical history. She reported that she was recently diagnosed with hypertension, hypothyroidism, and hypokalemia, but she struggled to recall details about when these diagnoses were made, what doctors she saw, and what medications she had been taking. Four months ago, she was hospitalized for psychosis, diagnosed with major depressive disorder (MDD) with psychotic features, and subsequently treated with sertraline. Examination revealed short-term memory deficits, generalized bradykinesia, flat affect, and a distinct Cushingoid appearance.

Historical Context

Harvey Cushing, commonly known as the father of neurosurgery, was the first to describe a basophil tumor of the pituitary gland leading to hypersecretion of glucocorticoids. In his biography, he writes that one of his earliest patients had been in an asylum due to severe neuropsychiatric disturbances hypothesized to be related to pituitary dysfunction. Furthermore, later during his career, he failed to accurately diagnose a case of pituitary dysregulation and instead performed cerebellar surgery, leading to a patient death. From these cases on, Cushing was extremely vigilant about pituitary tumors. His vigilance paid off years later when he not only coined the term "Cushing's disease," but also was the first to describe the psychiatric disturbances associated with the disorder.

Today, the term "steroid dementia syndrome" refers to the spectrum of neuropsychiatric symptoms that occurs in response to chronic hypercortisolism. Cushing's syndrome often manifests as dementia-like symptoms (such as memory and concentration impairment) or may mimic psychiatric disorders such as MDD, generalized anxiety disorder (GAD), or mania. Short-term memory deficits in particular can be large barriers to care for patients with hypercortisolism.

Discussion:

What is the primary mechanism by which hypercortisolism impairs memory?

A) Decrease in medial temporal lobe blood flow

B) Differential activation of glucocorticoid receptors in the hippocampus

C) Water-retention-related expansion of ventricles

D) Decreased event-related action potentials in response to visual/auditory stimuli

Answer: B

While all of the above findings have been observed in relation to glucocorticoids, the primary mechanism believed to be responsible for memory changes in Cushing's syndrome is related to differential activation of glucocorticoid receptors in the hippocampus. Mineralocorticoid receptors (type I receptors) are highly expressed in limbic areas like the hippocampus and entorhinal cortex. They bind glucocorticoids with a higher affinity and appear to be associated with memory enhancement. On the other hand, glucocorticoid receptors (type II receptors) are present in the limbic system as well as subcortical and cortical structures, with a higher distribution in the prefrontal cortex. Glucocorticoids bind to glucocorticoid receptors with lower affinity and are believed to be correlated with memory impairment. Chronic and excessive exposure to cortisol results in a preferential activation of the glucocorticoid receptors, which attenuates neurogenesis particularly in the hippocampus and prefrontal cortex. This is believe to be a key mechanism of impaired short-term and working memory in Cushing's Syndrome.

While the bilateral hippocampal atrophy seen in Cushing's syndrome is often reversible with correction of the hypercortisolism, the influence of hypercortisolism on cognitive function can persist for years after achieving eucortisolism, potentially impairing long-term quality of life. Therefore, it is important to include neuropsychiatric evaluations as part of the long-term routine follow up for these patients.

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Advancements in the Treatment of Complex Regional Pain Syndrome (CRPS)

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Disclosure Statement: The authors have no financial relationships to disclose.

Abstract
Complex Regional Pain Syndrome (CRPS) is a debilitating chronic pain condition that typically affects one limb and develops following an injury, stroke, or surgery. Although the precise pathophysiology of CRPS remains unknown, the understanding and management of CRPS have improved in recent years. This literature review highlights recent advancements in treatment, including pharmacological and non-pharmacological treatment options. Particular attention will be given to emerging technologies such as invasive neuromodulation, ketamine therapy, and mirror therapy, which have shown promise as alternative treatments. The review will emphasize the efficacy of these options and their integration into multidisciplinary management strategies.

Introduction
Complex regional pain syndrome (CRPS) is a rare and debilitating chronic pain condition that most often arises after trauma and commonly affects a single limb. CRPS is associated with severe pain that is typically accompanied by swelling, allodynia, hyperesthesia, and changes in temperature and skin color (1). Estimates of CRPS incidence vary based on diagnostic criteria and the time elapsed since the inciting injury, but recent studies suggests that the estimated annual incidence of CRPS is 26.2 cases per 100,000 people per year, and the five-year incidence of CRPS in the United States is 0.07% (2,3). CRPS significantly affects women more than men, with a ratio of up to 4:1, and it increases with age, with the highest incidence occurring between the ages of 50 and 80 years (2). Furthermore, CRPS more commonly affects patients with pre-existing pain conditions, including Rheumatoid arthritis and migraines (4).

Historically, CRPS has been difficult to diagnose since there is no single test that can definitively confirm or rule out the condition. Instead, the diagnosis is made clinically, relying on clinical assessment and imaging or laboratory tests to exclude other similar conditions. The accuracy and consistency of CRPS diagnosis have significantly improved since the development of diagnostic criteria. The clinical diagnosis criteria for CRPS were initially established by the International Association for the Study of Pain (IASP) in 1994 and have been updated twice since then (2). The Budapest criteria is the most recent version, and it is based on pain that is disproportionate to the inciting injury/trauma associated with 2 or more positive symptoms in at least 3 of the 4 categories, which include sensory vasomotor, edema/sudomotor, and motor or trophic (1,4). Supportive findings for CRPS include bone demineralization, joint effusion, and soft tissue edema. However, these findings are nonspecific and may also occur in other similar conditions. Additionally CRPS is divided into two subtypes, Type I and Type II, based on the absence or presence of peripheral nerve damage, respectively (2,5).

Although the exact pathophysiology of CRPS is not fully understood, it is thought to arise from an abnormal inflammatory response, autonomic dysfunction, and central sensitization following an injury. In individuals with CRPS, there is an increased production of cytokines (TNF-alpha, IL-1, and IL-6) compared to healthy individuals (4).

This leads to neuroinflammation, which contributes to the onset and persistence of pain associated with CRPS (5). Dysfunction of the autonomic nervous system can alter blood flow to the affected area, causing swelling as well as changes in temperature and skin color. Centra sensitization refers to the increased sensitivity and excitability of spinal nociceptor neurons, which is thought to contribute to the hyperalgesia seen in CRPS (2).

CRPS has been traditionally managed using a combination of non-steroidal anti-inflammatory drugs (NSAIDS), opioids, antidepressants, and anticonvulsants (1,2,4). However, many of these drugs have demonstrated limited efficacy, and effective management of CRPS continues to pose significant challenges for physicians. This paper reviews new emerging treatment options for CRPS.

Methods
We search PubMed and Google Scholar for articles with the following terms and keywords: Complex Regional Pain Syndrome, CRPS epidemiology, CRPS diagnosis and treatment, CRPS prognosis, Transcranial magnetic stimulation, Spinal cord stimulation, and physiotherapy. Human studies published in English with full-text articles were included. We focused on publications from the last five years while also including relevant studies from before that period.

Neuromodulation
Neuromodulation devices, including spinal cord stimulators (SCS), have demonstrated efficacy in improving symptoms, reducing the need for oral medications, and enhancing the overall quality of life in CRPS patients. SCS is though to function via the "gate control theory," which was first described by Melzach and Wall (6,7). The theory outlines that stimulation of non-nociceptive myelinated fibers (A-beta fibers) results in decreased propagation of painful stimuli from small nociceptive fibers (A-delta and C fibers) (6). The SCS device consists of electrode leads, a pulse generator, and a programmer. The leads are placed in the epidural space and deliver electrical impulses that interfere with

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the propagation of pain signals traveling from the spinal cord to the brain (7). SCS is currently approved for chronic pain conditions, including CRPS.

While spinal cord stimulation (SCS) may not alter the progression of a disease, research indicates that it can significantly improve physical function and enhance quality of life (5). A systematic review that evaluation 19 RCTs found that perceived pain relief, pain scores, and quality of life were all rates 1B+, providing strong evidence in support of SCS use (8). Another meta-analysis identified four RCTs that included Spinal Cord Stimulation as a treatment of CRPS. Out of the four, two studies compared Low-frequency SCS (LF-SCS) with placebo, one study compared LF-SCS with conventional physical therapy, and one study compared LF-SCS with high-frequency spinal cord stimulation (HF-SCS) (9). These RCTs showed a significant reduction in reported pain levels, favoring LF-SCS over sham/placebo stimulation and conventional therapy (9). Although SCS shows great promise in the treatment of CRPS, more longitudinal evidence is required to demonstrate its effectiveness.

Ketamine

Ketamine is a widely used anesthetic agent that acts by antagonizing N-methyl-D-aspartate (NMDA) receptors (1,5,10). Although primarily used for inducing general anesthesia, there have been reports that ketamine infusion therapy can improve pain and physical function in CRPS.

The exact mechanism of action is unclear; however, ketamine is believed to reduce cortical hyperexcitability by enhancing GABAergic transmission (5,10). In addition, ketamine therapy may reverse the cortical neuroplastic changes and central hypersensitization seen in CRPS (5).

A clinical trial involving over 100 participants with CRPS indicated that a 4-day escalating subanesthetic dose of ketamine could effectively treat CRPS in the lower extremities (5,10,11). However, for upper extremities, more than 4 days of treatment may be necessary to achieve comparable pain relief. Another study indicated a significant pain reduction difference between subanesthetic dose ketamine therapy and placebo lasting up to 11 weeks (10,12). While subanesthetic doses of ketamine have been preferentially used for CRPS, one study utilized high-dose ketamine and midazolam in intubated patients. 85 percent of patients reported improved quality of life at the 6-month follow-up, and 50 percent reported complete resolution of pain after 10 years (13,14).

Despite these findings, further studies are necessary to determine the optimal dose and duration of ketamine infusion. While current results indicate that ketamine infusion treatment may be effective for short-term relief, there is still limited understanding of the long-term effects of ketamine therapy.

Mirror Therapy

Patients with CRPS frequently experience sensations and perceptions that are out of proportion to physical exam findings. Mirror therapy is a rehabilitation technique that shows promise in managing these symptoms (5). This approach utilizes a mirror to create a visual illusion of movement in the affected limb, which may help to rewire neural pathways, leading to reduced pain and improved motor function (5, 15). MRI brain comparison studies before and after treatment suggest that motor imagery training is associated with the reversal of maladaptive cortical neuroplastic changes (16).

One study with eight CRPS patients reported significant improvements in pain, hand function, and range of motion after practicing mirror therapy for 15 minutes twice daily over six weeks (1, 17). Additionally, a study analyzing the efficacy of mirror therapy in CRPS following distal radius fractures found significant pain relief and positional awareness in 83.3 percent of patients (18).

While other studies have shown less conclusive outcomes, mirror therapy remains an appealing treatment option due to its affordability and non-invasive nature (1). It is especially promising for patients with upper limb involvement. Nonetheless, long-term research is needed to improve its protocols, including duration and frequency.

Future Directions & Conclusions

Although our understanding of CRPS has improved in recent years, management continues to post a major challenge for physicians since only a few interventions have been evaluated in randomized control trials. Future research should focus on large-scale trials to refine protocols, determine optimal session duration, and ensure safety.

Emerging therapies such as SCS, ketamine therapy, and mirror therapy show promising results. However, the variability in response highlights the importance of integrating these therapies into multidisciplinary pain management programs to maximize patient outcomes and quality of life.

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Crossed ICA: Unique Anatomical Variant

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Introduction

Anatomical variants in cerebral vascular anatomy contribute to approximately 10% of medical errors, underscoring the importance of compre-hending these variations. However, their prevalence in the general population remains uncertain. Among common variants, about 80% of individuals show some degree of anterior artery asymmetry.[1]

One particular notable variant involves aplasia or hypoplasia of the A1 segment of the anterior cerebral artery (ACA). Postmortem examinations reveal hypoplasia in approximately 10% and aplasia in 1-2% of cases.[1,2] Angio-MR studies indicate hypoplasia of the A1 segment in around 3% and of the A2 segment in about 2% of cases.[1,3] In such instances, the contralateral A1 segment of the ACA becomes dilated, and bloody supply to the entire area is facilitated through a dilated anterior communicating artery.[1]

Understanding the developmental origins of these arteries provides insight into their variations. The internal carotid arteries (ICAs) originate from the third aortic arches, the dorsal aortae, and a primitive vascular network near the developing fore- and mid-brain. Initially, the ICAs divide into cranial and caudal divisions, with the former giving rise to the anterior cerebral artery, anterior choroidal artery, and middle cerebral artery. The anterior communicating artery forms from a merging vascular network connecting the two developing anterior cerebral arteries.[1] This developmental framework illuminates the anatomical variations observed in clinical practice.

Case

Patient is a 68 year old female with a past medical history of hypertension, diabetes who presenting with bizarre behavior and altered mental status at work. At that time she had a CT angiogram of the head and neck which revealed a left middle cerebral artery aneurysm. Patient underwent cerebral angiogram for evaluation of the intracranial aneurysm which revealed a slightly elongated left middle cerebral artery aneurysm measuring 4 x 2 mm. The decision at that time was to consider conservative management given the patient's acute presentation of altered mental status that was not related to the aneurysm. Patient made a very remarkable recovery in the hospital and she was discharged after a few years. Later, Patient had a follow up clinic discuss the finding of the cerebral angiogram.

Physical Exam

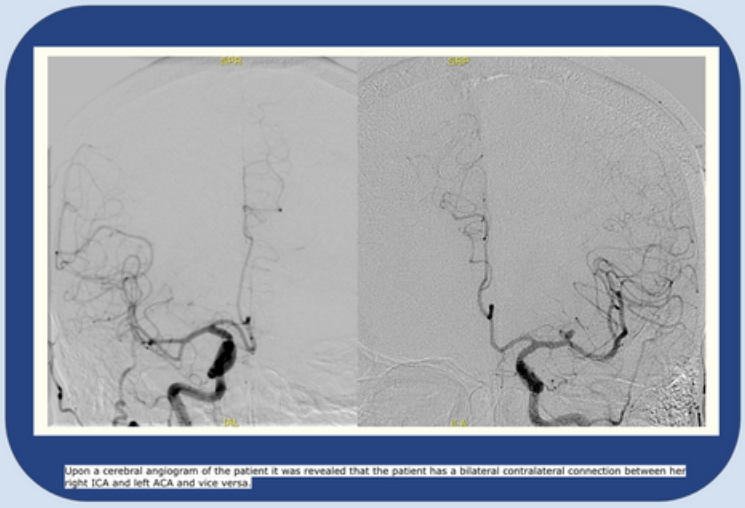
Allergies: N.K.A.Objective:Vitals: Ht: 5 ft 0 in, Ht-cm: 152.4 cm, Wt: 123 lbs, Wt-kg: 55.79 kg, BMI: 24.02, Body Surface Area: 1.54, BP Right: 130/75, Temp: 97.2 F, HR: 85. Examination: NEUROLOGY: Constitutional: well developed, well nourished, patient in no acute distress. Mental Status: alert and oriented. Head: normocephalic and atraumatic. Cortical Function: normal. Speech and language: normal. Cranial Nerves: normal. Motor Strength: 5 MRC. Sensory: normal pin prick arms and legs. Cerebellar: normal. Extrapyramidal: Patient with bilateral hand tremors.

Review of Systems

Eyes: Negative for:, Contacts, Positive for:, blurred vision, double vision. Ears, Nose, Mouth, Throat: Negative for: Deafness,Ringing,Swallowing,Hoarness. Cardivascular: Negative for:, chest pain,Edema,Skip Beats,Rapid Beats. Respiratory: Negative for:Cough,Cough W/Blood,Wheezing/Asthma,Shortness of Breath. Gastrointestinal: Negative for:, Hepatitis, constipation, diarrhea, blood in stool,fecal incontinence. Genitourinary: Negative for:, blood in urine, burning urination, incontinence,urinary frequency,scrotal swelling. Musculoskeletal: Negative for:Stiffness,Swelling,Muscle Weakness, Joint/Pain Arthritis,Backpain,Leg pain, Arm pain,Shoulder pain,Cane/Walker,Carpal tunnel, Osteoporosis. Integumentary (skin/breats): Negative for: brusing,lesions,birth marks. Neurological: Negative for: memory loss,mental status changes, tingling,paresthesia,seizure,spasms/ spasticity,weakness,speech difficulties, insomnia,suicidality, Positive for:, anxiety, depression, fatiguability. Endocrine: Negative for:, weight gain of greater than 20 lbs, weight loss of greater than 20 lbs.

Management

Patient was counseled on natural history and prognosis of brain aneurysm as well as stroke prevention. Patient was advised that based on the shape of the aneurysm interventional treatment was reasonable based on change in size/shape over time. Patient was told to follow up in two weeks regarding interventional options but was lost to follow up.



Upon a cerebral angiogram of the patient it was revealed that the patient has a bilateral contralateral connection between her right ICA and left ACA and vice versa.

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Crossed ICA: Unique Anatomical Variant

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Discussion

The presence of the bilateral contralateral connection between the internal carotid artery (ICA) and the anterior cerebral artery (ACA) significantly amplifies the risk of ischemia in the frontal lobe during endovascular procedures, particularly those conducted in the region of the anterior communicating artery (ACom A).[2,3] This variant poses a unique challenge due to the potential for inadvertent occlusion or disruption of critical blood flow pathways, which can precipitate ischemic events with profound neurological consequences. Furthermore, during endovascular procedures, there exists a heightened risk of medical error, as clinicians may misinterpret the anomalous vascular anatomy, mistakenly assuming vessel puncture or incorrect route navigation.

The underlying rationale for such anatomical variation often involves a spectrum of factors, including the presence of hypoplastic ICA with compensatory functional collaterals.[4,5] This scenario underscores the intricate interplay between developmental anomalies and adaptive mechanisms within the cerebral vasculature. Variants characterized by abnormal annealing, regression, or collateralization further contribute to the complexity of the vascular architecture, rendering it susceptible to misinterpretation and procedural challenges. While scenarios like this can be congenital, it is also feasible that the abnormal anatomy developed as a result of vascular remodeling due to her chronic hypertension.[1–5]

Essentially, any deviation from the typical vascular pattern can introduce variability and uncertainty, necessitating meticulous pre-procedural planning and intraoperative vigilance. Clinicians must possess a comprehensive understanding of cerebral arterial variants, their potential ramifications, and strategies for mitigating associated risks.

By incorporating this knowledge into clinical practice, healthcare providers can enhance patient safety, optimize procedural outcomes, and minimize the likelihood of adverse events in the context of neurointerventional procedures. Thus, a nuanced appreciation of the intricate vascular anatomy and its potential variations is indispensable for delivering high-quality, patient-centered care in neurosurgical and interventional neurology settings.

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A Case of Gelastic Seizures

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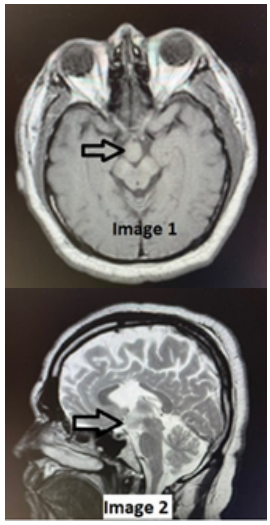
Case History

The patient is a 36-year-old man with a history of seizures from birth. The earliest episode that he could recall was one in which he began laughing and his eyes began watering because of which his parents took him to the doctor. Subsequently he began having what he described as a "scary feeling" in his upper chest followed by giggles for 2-3 seconds. These continued, some with loss of awareness and some others progressing to generalized tonic-clonic seizures between 9-18 years of age, despite multiple medications. At 18 he was seen in Phoenix, where he was diagnosed with a tumor in his hypothalamus, part of which was removed.



He had no family history of seizures. He was born full term by normal delivery and thrived normally afterwards. His develop-mental milestones were normal. He did not have any major childhood illnesses. His medical problem as an adult was limited to his seizure disorder. He did no report any history of head trauma with traumatic amnesia or loss of consciousness. He never smoked, used alcohol nor take any street drugs. His surgical history was limited to the brain surgery noted above, followed by a Gamma Knife surgery later and a VNS implantation in 2021. On general exam-mination he was noted to be a mildly obese adult male, in no acute distress with a negative musculoskeletal survey and without evidence of neurocutaneous lesions. The neurological examination was completely normal. The arrows in the Axial (T1 SE) and the sagittal (T2FRSE) images point to the lesion in Images 1 and 2 to the right.

Discussion

Image 1 on Page 1 shows the pre-peduncular location of the lesion and Image 2 shows the lesion within the hypothalamus which on biopsy was found to be a hamartoma. Hamartomas are benign tumors that can occur anywhere in the body. Hypothalamic hamartomas (HHs) are rare but characteristically present with "laughing spells" as in the case of the patient described on Page 1.

Gelastic seizures represent a rare manifestation of epilepsy. It was initially desribed in 1957. The laughter is considered mechanical rather than emotional. Seizure frequency varies and up to 200 per day have been observed. Patients may develop complex partial seizures, drop attacks, and generalized tonic-clonic seizures as well in due course. Behavioral problems including aggression and cognitive deterioration with intellectual deficiency may also occur.

At least 3 different classifications based on the gross appearance and location of the tumor and the MRI features have been proposed. Based on the anatomic location and seating, these tumors have been classified into peduncular and sessile or intraparenchymal. Based on MRI, it has been suggested that the parahypothalamic type attached to its floor with a peduncular process is associated with the precocious puberty which may occur in up to 50% of children whereas the sessile (intrahypothalamic) HHs with or without ventricular extension more commonly cause gelastic epilepsy, the phenomenon being more frequent with the latter due to its proximity to the thalamus as it extends into the third ventricle. The rare phenomenon of dacrystic (crying) seizures where the patients lets out a scream have also been reported with these tumors. The sessile HHs may or may not be associated with precocious puberty.

HHs can occur as isolated lesions or be part of syndromes such as Pallister-Hall syndrome, oral-facial-digital syndromes, and Bardet-Biedl syndrome among others. GLI3 mutations have been reported in a small number of isolated and syndromic cases of HHs.

Pathologically the tumors may contain tissues belonging to all three layers of the embryo, namely the endoderm, mesoderm and the ectoderm. Microscopically, the cells resemble the tissue of origin in HHs and grow at the same rate as the tissue of origin unlike choristomas which grow in non-homologous tissues.

The mainstay of treatment is the use of antiseizure medications, which are often ineffective in controlling gelastic seizures due to HHs. Surgical resection can be curative or may be helpful in reducing the seizure burden. Radiosurgery and MRI-guided laser interstitial thermal therapy are effective alternatives to traditional surgical approaches or may supplement traditional surgery.

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Post-Thymectomy Onset of Morvan Syndrome in a Patient with Preexisting Isaac's Syndrome: A Case Report and Literature Review.

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Introduction

Anti-voltage-gated potassium channel (VGKC) complex antibodies, such as contactin-associated protein-like 2 antibodies (CASPR2-Ab) and leucine-rich glioma inactivated protein 1 antibodies (LGI1-Ab), have been linked to a range of neurological symptoms affecting both the peripheral and central nervous systems (1). Isaacs' syndrome primarily presents with peripheral symptoms such as neuromyotonia caused by peripheral nerve hyperexcitability. In contrast, Morvan syndrome encompasses 1) central nervous system issues, such as neuropsychiatric disturbances and insomnia; 2) autonomic symptoms, like diffuse sweating and arrhythmias; and 3) peripheral nerve hyperexcitability (1,2).

Anti-VGKC complex antibody disorders are often paraneoplastic, with thymoma present in roughly one-third of cases (1-3). Although thymectomy remains the standard treatment, some studies report that post-thymectomy patients experience either worsening of Morvan syndrome or, in some instances, new onset of the condition (4-10).

In this report, we discuss a notable case of Isaacs syndrome that progressed to Morvan syndrome following thymectomy. Alongside this case, we aim to deliver an extensive literature review on studies that highlight the development of Morvan syndrome in patients post-thymectomy, thereby enhancing our understanding of post-thymectomy outcomes.

Case description

A 49-year-old Caucasian woman with past medical history of stage 2 breast cancer s/p mastectomy and sarcoidosis presented with pain and muscle twitches in all four limbs, along with leg muscle spasms and cramps that had begun 2-3 years before this presentation. She reported no sensory symptoms, cognitive changes, or sphincter dysfunction. Neurological examination revealed normal mental status and cranial nerve function, with no muscle bulk abnormalities. However, frequent muscle twitches were observed in her limb muscles, and she displayed poor muscle relaxation in her arms and legs without clear signs of spasticity or rigidity. Sensory examination was normal, deep tendon reflexes were 2+ throughout, and her gait was slightly stiff and antalgic. Romberg's test was negative. Electromyography (EMG) showed myokymic discharges in the form of doublets, as well as fasciculations in all limbs (Figure 1a). This raised concern for peripheral hyperexcitability syndrome.

Serum analysis indicated positive LGI1 (1:640, reference range <1:10) and CASPR2 antibodies (>1:2560, reference range <1:10), subtypes of VGKC complex detected through indirect immunofluorescence assay, confirming the diagnosis of Isaacs syndrome. Treatment was initiated with a 5-day course of intravenous immunoglobulin (IVIG) at 0.4 mg/kg/day alongside carbamazepine. A thorough search for underlying neoplasms was conducted. Thoracic CT revealed an anterior mediastinal mass measuring 26 x 25 x 46 mm^3, consistent with a thymoma (Figure 1b). She was diagnosed with type B3 thymoma with invasion into surrounding structures per the Masaoka staging system, and thymectomy was performed two weeks later, involving resection of the mediastinal pleura and pericardium, which pathologically revealed a type B3 thymoma according to the World Health Organization criteria (Figure 1c). Concurrent myasthenia gravis was ruled out with negative anti-acetylcholinesterase antibodies.

One-week post-thymectomy, the patient developed new symptoms, including confusion, memory disturbances, visual hallucinations, insomnia, diaphoresis, and labile blood pressure. She continued to display fasciculations and myokymia upon examination. Electroencephalogram (EEG) findings showed moderate diffuse encephalopathy. Given the onset of neuropsychiatric and autonomic symptoms alongside peripheral neuromyotonia, she was diagnosed with Morvan syndrome in a post-thymectomy patient with preexisting Isaac's syndrome. Treatment with a 5-day course of plasmapheresis was administered, resulting in gradual symptoms improvement over the following two weeks. The patient was discharged from the hospital four weeks after thymectomy. At her two-month follow-up, her muscle twitches had improved, though she still experienced intermittent confusion. Repeat anti-VGKC antibody titers were negative; LGI1 was 1:5 (reference range <1:10) and CASPR2 and 1:1 (reference range <1:10), indicating disease remission.

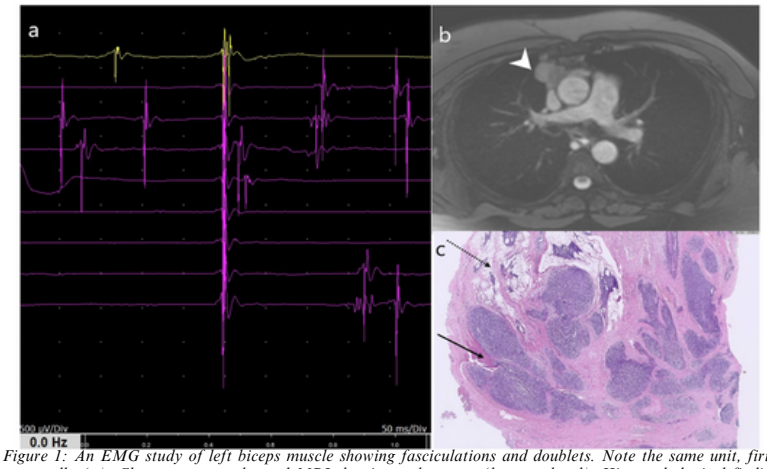

Figure 1: An EMG study of left biceps muscle showing fasciculations and doublets. Note the same unit, firing repeatedly (a). Chest contrast-enhanced MRI showing a thymoma (b, arrowhead). Histopathological findings of thymoma abundant lymphocytes and neoplastic epithelial cells invading into surroundings mediastinal structures (c, solid arrow) and normal thymic tissue (c, dotted arrow).

Discussion

Anti-VGKC complex antibody-mediated disorders exhibit a broad range of neurological symptoms affecting both the peripheral and central nervous systems. These include Isaacs syndrome, marked by peripheral nerve hyperexcitability, and Morvan syndrome, which is characterized by a combination of peripheral nerve hyperexcitability, encephalopathy, and autonomic dysfunction (1,2). The presence of anti-LGI1 antibodies is often linked to neuropsychiatric symptoms, while anti-CASPR2 antibodies are known to be paraneoplastic, mostly secondary to thymoma or small cell lung cancer (1,2). Nevertheless, both anti-LGI1 and anti-CASPR2 antibodies can be positive in cases of Isaacs or Morvan Syndrome (1,5).

Our patient initially presented with diffuse fasciculations and myokymia, along with positive anti-VGKC complex antibodies, leading to a diagnosis of Isaacs syndrome. Shortly after undergoing thymectomy, the patient developed central nervous system symptoms, including confusion

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hallucinations, agitation, and insomnia, as well as dysautonomia symptoms characteristic of Morvan syndrome. Plasmapheresis was subsequently administered, resulting in symptom improvement.

Morvan syndrome occurs as a paraneoplastic process in up to one-third of cases, most often linked to thymoma and, less commonly, small cell lung cancer (1). Thymectomy is the standard treatment, though some studies indicate that post-thymectomy patients may experience worsening or even new onset of Morvan syndrome (4-10). Similar to our patient, one recent study documented a 49-year-old Japanese male with Isaacs syndrome who, after thymectomy, developed Morvan syndrome two months later. (5) Other reports also note symptom exacerbation following thymectomy in Morvan syndrome cases (4,6).

This phenomenon is not exclusive to peripheral hyperexcitability syndromes. Thymoma is also associated with a broad range of autoimmune paraneoplastic syndromes (PNs) like myasthenia gravis, limbic encephalitis, good's syndrome, autoimmune thyroid disorders, autoimmune hepatitis, and various cutaneous autoimmune diseases (8). In many cases, patients with these autoimmune PNs developed typical Morvan syndrome symptoms post-thymectomy (7-10). Table 1 summarizes studies reporting onset/worsening of Morvan syndrome after thymectomy.

Table 1: Case studies which reported post-thymectomy onset of Morvan syndrome

Case	Age/Sex	Indication for thymectomy	Stage	Interval between thymectomy and onset / worsening of Morvan syndrome	Treatment recieved	Improvement of symptoms (in days)
Our case	42/F	Isaac's syndrome	3B	1 week	PLEX	2 weeks
Suzuki et al. [5]	48/M	Isaac's syndrome	2B	8 weeks	mPSL, PLEX	4 weeks
Cottrell DA et al. [4]	70/M	Thymoma	NA	6 weeks	mPSL, PLEX	2 weeks
Maskery M et al. [6]	74M	Morvan syndrome	AB	1 week	mPSL, PLEX, IVIG, azathioprine	12 weeks
Oh S et al. [7]	67/M	Myasthenia gravis	NA	16 weeks	Gabapentin, carbamazepine	No improvement, palliative care
Liu H et al. [8]	49/M	Myasthenia gravis	2B	24 weeks	IVIG, Rituximab	4 weeks
Galie E et al.[9]	35/M	Thymoma	4A	4 weeks	IVIG	NA
Banks KC et al.[10]	40/M	Thymoma	3B	NA	IVIG, Rituximab	NA

Abb: PLEX - plasmapheresis; mPSL- methylprednisolone; IVIG - intravenous immunoglobulins

The underlying mechanisms behind the onset of Morvan syndrome following thymectomy remain uncertain. One hypothesis suggests that thymectomy may expose hidden antigens or change the immune environment, leading to increased levels of pathogenic antibodies like anti-LGI1 and anti-CASPR2 (4,6). Additionally, the thymus plays a critical role in immune regulation, and its removal could disrupt immune tolerance, potentially increasing autoantibody production (4,6).

While it's unclear if thymectomy directly triggers new or worsened cases of Morvan syndrome, published case reports indicate that this risk cannot be ignored. Patients should be informed of the potential for developing or worsening Morvan syndrome symptoms post-thymectomy. Clinicians should remain vigilant, as symptoms in preexisting cases may intensify or new cases may emerge, potentially requiring repeated immunotherapy and ICU support. Early identification and treatment with immunotherapies, such as plasmapheresis or intravenous immunoglobulin, can improve outcomes and help prevent severe complications.

Conclusions

Peripheral hyperextensibility syndromes are often associated with paraneoplastic processes. However, the presence of an existing cancer, such as breast cancer in our patient, should not prevent further investigation for an additional underlying tumor. In this case, this peripheral hyperextensibility syndrome was linked to a thymoma rather than the pre-existing breast cancer.

While thymectomy is the standard treatment for thymoma-associated conditions, there is evidence suggesting it may precipitate or worsen Morvan syndrome in some patients. The exact mechanism remains unclear, but the potential risk underscores the need for careful patient selection, through preoperative discussions, and vigilant postoperative care.

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Author's contributions: N.T contributed to study conception and design, literature search, manuscript writing, preparation and submission. K.F. contributed study conception and design and manuscript editing.

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Peripheral Nerve Hyperexcitability Syndrome, Approach and current understanding of this diagnosis entity: A Case and literature review

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Disclosure: N/A

Abstract

Peripheral nerve hyperexcitability (PNH) syndromes are rare disorders characterized by excessive peripheral nerve activity, presenting as muscle fasciculations, cramps, and myokimia and neuromyotonia. This report describes a 46-year-old woman with muscle twitching, dysautonomia, and significant autoimmune markers, ultimately diagnosed with PNH with phenotype of Morvan syndrome (MoS). Elevated Voltage-Gated Potassium Channel (VGKC) complex antibodies and a thymic carcinoma further confirmed the diagnosis. Despite complications during immunotherapy and thymectomy, her symptoms improved with targeted treatment. This case underscores the need for standardized diagnostic criteria for PNH syndromes to facilitate early identification and improve outcomes. A literature review highlights gaps in classification and management of PNH subtypes.

Keywords: Myokimia, Neuromyotonia, Dysautonomia, CASPR2 antibodies.

Introduction

Peripheral nerve hyperexcitability (PNH) syndrome is characterized by spontaneous and excessive activity of the peripheral nerves, which may result in muscle hyperactivity and delayed muscle relaxation.[1] These manifests as muscle twitches, cramps and stiffness. Electro physiologically they may manifest as fasciculations, myokymia or neuromyotonia.[1] PNH can be classified into three categories based on etiology: immune-mediated PNH, inherited PNH, or idiopathic PNH. Immune-mediated PNH syndromes involve IgG antibodies against axonal voltage-gated potassium channels, such as CASPR2 (contactin-associated protein-2) and LGI1 (Leucine-rich glioma-inactivated 1).[2] Electrodiagnostic workup, including needle electromyography (EMG), may demonstrate neuromyotonic discharges with spontaneous repetitive single motor unit action potentials.

PNH syndromes may have been categorized into three primary types in the literature: cramp-fasciculation syndrome (CFS), Isaacs syndrome, and Morvan syndrome (MoS). While these syndromes share overlapping clinical, immunological, and electromyographical features, they are distinguished by differences in disease severity and associated symptoms.[2] For example, CFS is primarily characterized by fasciculations in the peripheral nervous system, with normal motor unit action potential morphology and recruitment on EMG.[3] Isaacs syndrome manifests as persistent myokymia and neuromyotonia, which may be linked to autoimmune or paraneoplastic mechanisms.[3] MoS is a combination of peripheral nerve hyperexcitability with central nervous system involvement and autonomic dysfunction and may be associated with paraneoplastic mechanisms.[2] Antibodies, especially CASPR2, are more commonly linked to Isaacs syndrome and MoS, especially in the presence of malignant thymoma.[4] There is a paucity of literature that further differentiates the major PNH syndrome subtypes in aspects like management and prognosis. There is a lack of consensual guidelines and specific diagnostic criteria to further characterize these clinical entities.

In this report, we describe a case of a female patient muscle twitching. Systematic work up and a multitier approach of investigations led to the diagnosis of PNH. Our unique case report highlights the need for standardized diagnostic criteria that may facilitate early diagnosis of PNH syndromes. We believe that this criterion will optimize both short-term and long-term outcomes by allowing timely intervention for PNH syndrome.

Case presentation

A 46-year-old African American woman was presented to the Emergency Department for tachycardia and generalized weakness. She was experiencing muscle twitching and flickering movements in her extremities and face for 4 months. She also reported occasional bilateral painful muscle spasms in her lower extremity. This was aggravated by exercise, especially long-distance walking. She experienced anorexia, resulting in an unintentional weight loss of 50 lbs, and insomnia, requiring 75 mg of pregabalin twice daily. Her past medical history was significant for sarcoidosis with frequent flares and left breast cancer. Previously, she was admitted twice with the same complaints with normal diagnostic workup, including non-significant EEG. She was discharged with cyclobenzaprine and baclofen without any significant improvement in her symptoms.

On physical examination, the patient presented with sinus tachycardia. Neurological evaluation revealed fasciculations in the bilateral quadriceps, right hamstrings, left biceps, and tongue,

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along with small areas of tongue atrophy. Hyperreflexia was noted in the upper extremities, while reflexes in the lower extremities were normal. She exhibited occasional flickers in the arm and perioral muscles, painful spasms, and delayed relaxation after voluntary contractions of hand muscles.

On diagnostic workup, her complete blood count and comprehensive metabolic panel were within normal range except for creatinine (1.72 mg/dL; normal: 0.5-1.04) and ESR (89 mm/hr; normal:2-30). Her thyroid function test was normal. An EKG confirmed sinus tachycardia with normal serum cardiac biomarkers. An autoimmune panel showed a positive antinuclear antibody (ANA) with an SSA/Ro pattern at a low titer of 1:320 (significant titers > 1:160). Serum-ionized calcium (5 mg/dL; normal: 4.5-5.3) and angiotensin-converting enzyme (ACE) levels 20 U/L; normal: 16-85) were within the normal range. Her chest X-ray was normal, with no hilar lymphadenopathy, collectively ruled out flaring of sarcoidosis. Her CSF analysis results were non-significant without any oligoclonal bands (Table 1) except for positive autoimmune markers (Table 2) which was suggestive towards a hyperexcitable nervous system disorder, though motor neuron disease could not be entirely excluded. Serum autoimmune panel revealed significantly elevated Voltage-Gated Potassium Channel (VGKC) IgG antibodies at 910 pmol/L (reference range: 2-30), along with positive results for CASPR2 (contactin-associated protein-2) IgG and LGI1 (leucine-rich glioma-inactivated 1) IgG antibodies (Table 2). Further diagnostic workup including paraneoplastic panel was normal (Table 3). Structural abnormalities of the temporal lobe or evidence of limbic encephalitis were ruled out by non-significant findings on brain MRI. EEG revealed no epileptiform discharges which ruled out seizures. Needle electromyography identified diffuse fasciculations, doublets, triplets, and myokymia in the left upper and lower extremities, without evidence of neuropathic or myopathic potentials (Table 4). This diagnostic workup confirmed the presence of PNHS. The patient fulfilled all four major criteria proposed by Watanabe et al. and was diagnosed with definite acquired paraneoplastic neuromyotonia/PNH syndrome.[5] A CT scan of soft tissue neck, chest, abdomen, and pelvis without contrast revealed an ovoid nodule in the right anterior mediastinum (2.5 x 1.8 cm), which circumscribed margins and homogenous attenuation, suspicious for thymic epithelial tumor. MRI of the chest suggested a potential early invasive thymic carcinoma.

The patient was started on combination of immunomodulation and membrane stabilizing therapies with Intravenous Immunoglobulin (IVIG), Clonazepam (1 mg twice daily), and Oxcarbazepine (150 mg twice daily). She reported mild improvement in fasciculations after a 5-day course of IVIG. Following IVIG, therapeutic plasma exchange (PLEX) was initiated. After her first PLEX session, her hospital course was complicated by acute hemolytic anemia, necessitating temporary discontinuation of PLEX therapy. She required a blood transfusion, and PLEX therapy resumed after five days. Significant improvement in her fasciculations and twitching was noted after three sessions of PLEX.

A CT-guided fine needle aspiration biopsy revealed thymic carcinoma with positive CD99, TdT and Ki-67 biomarkers on immunohisto-chemical staining, indicating a high proliferation index (~50%). The patient was consented for thymectomy. On exploration, locally advanced tumor was noted invading into the surrounding structures requiring en bloc resection of pericardium, phrenic nerve, and superior vena cava, and diaphragm plication. The surgical specimen biopsy confirmed a diagnosis of Type B3 thymoma. Her postoperative course was complicated by intrathoracic bleeding requiring transfer to surgical intensive care unit. We suspected that PLEX therapy might have contributed to bleeding. On discontinuing PLEX therapy, her mental status deteriorated, with waxing and waning confusion. After ruling out acute etiologies, we hypothesized that worsening of her existing PNH may have contributed to her altered mental status. PLEX session was resumed for the last two sessions following which her mental status improved.

In summary, neuromyotonia associated with CNS depression, persistent insomnia, dysautonomia with tachycardia and biopsy-proven thymoma, confirmed a diagnosis of PNH with a phenotype of Morvan's syndrome. The patient later underwent adjuvant chemoradiotherapy for thymoma, which resulting in significant improvement in neuromyotonia.

Table 1: *Cerebrospinal Fluid (CSF) analysis*

CSF component	Results	Reference Range
Cell Count	17 cells/uL	
Segs%	29%	0-7%
Lymphs%	71%	28-96%
Glucose	63 mg/DL	50-80
Protein	43 mg/	
Gram stain	Negative, No PMNs or Mononuclear cells	
CSF culture	No organisms isolated	

CSF, cerebrospinal fluid; PMN, polymorphonuclear

Discussion

Peripheral nerve hyperexcitability disorders are a rare heterogenous entity. There is a lack of consensual diagnostic criteria that make the identification of these disorders difficult. The most common clinical presentation based on longitudinal cohort studies were muscle twitching muscle cramps, muscle pain, and neuromyotonia which manifests clinically as difficulty releasing handgrip.[6] Some patients also present with dysautonomia features like sleep disorders, fluctuations in blood pressure and heart rate, gastrointestinal symptoms and excessive sweating.[6,7] Central nervous system manifestations like agitation, lethargy, and seizures are seen in a minority of cases.[6] Despite this clear description of the presentation, the diagnosis of these patients remains uncertain and is one after exclusion. One of the patients earliest studies by Watanabe defined criteria for Issac syndrome. These criteria included both clinical and electrodiagnostic evidence of neuromyotonia (difficulty releasing

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hand grip) in the absence of percussion myotonia, electromyographic evidence of nerve excitability like myokymia, presence of antibodies to Voltage-gated potassium channel complex, and response to immunotherapy. However, there were no further studies that attempted at validating the criterion for the other entities of this category of peripheral nerve hyperexcitability disorders.

Conclusions

Peripheral nerve hyperexcitability disorders are rare and distinct groups of disorders leading to significant morbidity and suffering. Symptoms can often be nonspecific. Strong index of suspicion can help investigate and diagnose this condition promptly. The lack of consensual diagnostic criteria makes prompt diagnosis more difficult.

Table 2: *Autoimmune panel testing*

Autoimmune Panel	Result	Reference interval
NMDA Receptor Ab IgG CBA-IFA, Serum & CSF	Negative	<1:10
CASPR2 Ab IgG CBA-IFA Screen, Serum CSF	Detected >1:2560 1:10	<1:10
LGI1 Ab IgG CBA-IFA Screen, Serum CSF	Detected 1:640 1:50	<1:10
NMO/AQP4 Ab IgG CBA-IFA Screen, Serum & CSF	Negative	<1:10
AMPA Receptor Ab IgG CBA-IFA Scrn, Sereum & CSF	Negative	<1:10
GABA-BR Ab IgG CBA-IFA Scrn, Serum & CSF	Negative	<1:10
GABA-AR Ab IgG CBA-IFA Screen, Serum & CSF	Negative	<1:10
DPPX Ab IgG CBA-IFA Screen, Serum & CSF	Negative	<1:10
MOG Ab IgG CBA-IFA Screen, Serum & CSF	Negative	<1:10
IgLON5 Ab IgG CBA-IFA Screen, Serum & CSF	Negative	<1:10
mGluR1 Ab IgG CBA-IFA Screen, Serum & CSF	Negative	<1:10
Voltage-Gated Potassium Channel Ab, Serum CSF	 910 pmol/L H 1.1 pmol/L	 0-31 0.0-1.1
Glutamic Acid Decarboxylase Antibody	<5.0 IU/mL	0.0-5.0
Acetylcholine Binding Antibody	0.0 nmol/L	0.0-0.4
MuSK Ab IgG CBA IFA Screen, Serum	Negative	<1:10
Acetylcholine Modulating Antibody	0%	<=45

IgG, Immunoglobulin G; Ab, Antibody; CBA-IFA, Cell Binding Assay-Immunofluorescence Assay; CSF, cerebrospinal fluid; NMDA, N-methyl-D-aspartate; CASPR2, Contactin-associated protein-like 2; LGI1, Leucine-rich, glioma inactivated 1; NMO/AQP4, Neuromyelitis Optica/ Aquaporin-4; AMPA, A-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; GABA-BR, gamma-aminobutyric acid B receptor; GABA-AR, gamma-aminobutyric acid A receptor; DPPX, Dipeptidyl-peptidase-like protein-6; MOG, Myelin oligodendrocyte glycoprotein; IgLON5, Immunoglobulin-like fifth member of Limbic System-associated Membrane Protein family; MGluR1, metabotropic glutamate receptor 1; MuSK, Muscle-Specific Kinase.

Table 4: *Needle electromyography*

EMG

Side	Muscle	Nerve	Root	Ins Act	Fibs	Fasc	Amp	Dur	Poly	Recrt	Disch	Comment
Left	Abd Poll Brev	Median	C8-T1	Nml	0	0	Nml	Nml	<15%	Nml	0	
Left	1stDorInt	Ulnar	C8-T1	Nml	0	1+	Nml	Nml	<15%	Nml	0	
Left	Biceps	Musculocut	C5-6	Nml	0	2+	Nml	Nml	<15%	Nml	0	Myokymia,
Left	Triceps	Radial	C6-7-8	Nml	0	3+	Nml	Nml	<15%	Nml	0	Myokymia,
Left	AntTibialis	Dp Br Peron	L4-5	Nml	0	2+	Nml	Nml	<15%	Nml	0	Myokymia,
Left	Peroneus Long	Sup Br Peron	L5-S1	Nml	0	2+	Nml	Nml	<15%	Nml	0	
Left	Gastroc	Tibial	S1-2	Nml	0	2+	Nml	Nml	<15%	Nml	0	Myokymia
Left	VastusMed	Femoral	L2-4	Nml	0	3+	Nml	Nml	<15%	Nml	0	Myokymia,
Left	VastusLat	Femoral	L2-4	Nml	0	2+	Nml	Nml	<15%	Nml	0	Myokymia,
Left	FlexCarRad	Median	C6-7	Nml	0	1+	Nml	Nml	<15%	Nml	0	
Left	Deltoid	Axillary	C5-6	Nml	0	1+	Nml	Nml	<15%	Nml	0	

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Bridging Language Gaps in Bedside Neurological and Stroke Examination for Patients with Limited English Proficiency

Ivan Trang, MD; Amir Ali, MD; Ganne Chaitanya, MD PhD; Thy P. Nguyen, MD; Anjail. Z. Sharrief, MD, MPH

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In Texas, about 3.6 million people (12.82% of the population) have limited English proficiency (LEP), a factor that can lead to lower quality medical care and delays in code stroke evaluation. To address this challenge, our team is developing a multilingual mobile application to streamline bedside neurological examinations and the administration of the National Institutes of Health Stroke Scale (NIHSS). We are also creating a training course to teach clinicians how to perform these assessments in Spanish. Our preliminary data highlights the urgency of this initiative. In a survey of clinicians evaluation patients with LEP during code strokes, 77% (17/22) reported difficulties with translation device availability, and 73% (16/22) encountered technical difficulties with translation devices. Furthermore, 84% of clinicians and nurses expressed interest in learning to perform the NIHSS in another language, signaling a strong demand for such tools and training. We presented these results at the SVIN 2024 Annual Meeting and will be presenting additional results at the International Stroke Conference 2025. Progress to date includes complete Spanish and Vietnamese translation of the NIHSS, an IRB application draft, and the submission of a UE5 grant proposal to secure additional funding and research time. Looking ahead, we plan to finalize the mobile application and pilot these innovations to improve care for LEP patients.

Multicenter Registry for Venous Sinus Stenting in IIH

Anqi Luo, MD

Objective
To examine the demographics and clinical outcomes of patients who underwent cerebral venous sinus stenting (VSS) for medically refractory idiopathic intracranial hypertension (IIH) across two tertiary hospitals in the United States.

Background
IIH is characterized by increased intracranial pressure, commonly presenting with headaches, visual disturbances, and pulsatile tinnitus. Traditional surgical intervention involves cerebrospinal fluid diversion, but many patients require shunt revision. While cerebral VSS is emerging as an alternative, large multicenter studies, particularly those identifying predictors for repeat stenting, remain limited.

Design/Methods
A retrospective analysis was conducted on IIH patients treated with VSS at two tertiary hospitals from 2012 to 2024. Demographics, baseline clinical characteristics, and clinical outcomes were evaluation for up to 12 months post-treatment.

Results
Among 168 IIH patients (mean age 39 years), 92.3% were female (n=155). The mean pressure gradient across the stenosis decreased significantly from 14.96 pre-stenting to 1.28 mmHg post-stenting (P<0.001). Headaches (86.4%) and pulsatile tinnitus (69.7%) improved post-stenting. Papilledema, using Frisen grading, decreased significantly in both eyes from 68.9% to 34% post-stenting (P<0.001). Repeat stenting occurred in 18 patients (10.7%) and was significantly more likely in those with stent adjacent stenosis (P<0.001). Initial tinnitus (P=0.03) was a significant predictor of requiring repeat stenting. Higher BMI (P=0.20) and left-sided stenosis (P=0.12) were associated with repeat stenting but were not statistically significant. Stent type did not have a significant impact on repeat stenting (P=0.21).

Conclusions
Our preliminary data suggest that VSS is effective for medically refractory IIH and carries a low risk of repeat stenting. We hypothesize that higher BMI, tinnitus as the main symptom, and left-sided venous sinus stenosis may be predictors for requiring repeat stenting. Our study is ongoing, and we will confirm these findings upon its completion.

Neurology Education Utilizing Resident Opinions on Strategies (NEUROS)

Kelsey Cacic, MD

Adult Learning Theory (ALT) has changed the way we understand adult learners but has yet to fully penetrate the way we teach our medical residents. Whereas medical education is often steeped in lengthy didactic sessions, ALT suggests education should emphasize self-directed learning, collegial inquiry, teamwork, and, more recently, gamification. Game elements and mechanisms used in the education environment encourage learners, motivate action, and promote learning. While this has been proven effective in casual engagement, the impact on practical application is uncertain and can be difficulty to implement with a large curriculum, diverse learners, and a short time period to gain standardized knowledge. The aim of NEUROS is to incorporate the tenants of the ALT during a week-long neurology "bootcamp" for new residents with an emphasis on gamification into didactic sessions and solicit learner feedback to modify sessions in an iterative process, focused on promoting learner engagement, confidence, and practical application. This has been broken into four phases that repeat annually over the next three-to-four years. As of December 2024, phases 1-3 have been completed for the first year with phase 4 beginning in late December - early January 2025.

Phase 1 was the pre-course survey which asked the learner to self-evaluate their confidence is a variety of topics, including: performing and interpreting a neurological exam, reading an EEG, assessing and treating status epilepticus, interpreting neuroradiology, managing common neurological emergencies such as stroke and neuromuscular crises, and evaluation a variety of common outpatients complaints. The survey also included didactics preferences such as lecture length, modality, and perception of gamification. All questions were rated on a 1-5 point scale. The 2024 pre-course survey was notable for low confidence in areas expected for new neurology residents: reading EEGs, interpreting neuroradiology, managing stroke alerts, and management neuromuscular emergencies. Learners reported high confidence in performing a neurological exam for lower confidence in interpreting their exam. In terms of educational modalities, learners largely noted a preference for shorter lectures, interactive content, and felt that gamification would increase collaboration.

Phase 2 was the week-long course which includes optional self-directed online learning, high-fidelity simulations, standardized patients, and didactics enhanced with elements of gamification. Four different simulations were run that were paired with related didactic sessions on the following topics: stroke, seizures, brain death, delivering bad news. Standardized patients, with a variety of diagnoses, were utilized to allow learners to practice their exam and interpretation in a safe and proctored environment. Lastly, the gamification was initially incorporated during

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Neurology Education Utilizing Resident Opinions on Strategies (NEUROS)

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the 2024 course by dividing the learners into teams which worked together to answer questions built into the otherwise standard didactic sessions. The team with the most points at the end of the day won prizes. On the afternoon of the last day of the course, a game-show style quiz was played by the teams which incorporated questions from throughout the course.

Phase 3 was the post-course survey that mirrored the pre-course survey. The 2024 post-course survey was notable for increased confidence in both exam performance and interpretation increased post-course by an average of 1 point (on a 5-point scale). Learners additionally had at least 1.5-point (on a 5 point scale) increase in confidence in several covered subject areas: reading EEGs, treating status epilepticus, treating neuromuscular emergencies, managing strokes, assessing for Parkinson's disease, and managing epilepsy. In terms of educational modalities, most learners felt that 1-1.5 hour didactics sessions were an appropriate length. They additionally felt that the "gamification" aspect kept them engaged, increased networking and collaboration, and enhanced learning.

For the upcoming phase 4, learners will be asked to complete a survey looking back retrospectively at the bootcamp curriculum. The surveys will assess whether they feel the curriculum increased their knowledge and confidence in the material, was presented in a way that had clear practical application, and whether gamification helped with material retention. That feedback will be used, in an iterative process, to improve learning and didactics for the next year's class. A first test set of surveys were sent out at 3 months with poor response rate. As the first year of neurology residency is busy, this is an expected barrier. To improve response rates as the desired 6-month follow-up, incentives will be offered for participation.

Based on current feedback from phases 1-3, tentative changes to the course for the 2025 cycle include more formalized gamification of didactics and increased interactive sessions. In particular, a standardized slide set will be used for gamification questions to ensure continuity across lectures and white boards will be provided to teams to assist with collaboration. Additionally, several of the standard didactics sessions that previously were not well suited to gamification will be converted into itneractives sessions. Further modifications to the course will be determined after the completion of phase 4 in Jan2025, after which the cycles (phase 1-4) will be repeated for the class of 2025.

A Novel Approach to Expedite Acute Stroke Triage in Texas

Jerome Jeevarajan, MD

Background

Stroke is the third leading cause of death in Texas, and acute ischemic stroke remains the most common stroke subtype. Endovascular therapy (EVT) has been shown to improve outcomes for select patients with stroke due to large vessel occlusion (LVO), but more than half of patients still have significant disability after treatment. This is exacerbated by the lack of immediate access to specialized care in the neurologically underserved areas of Texas.

For patients being emergently evaluated for LVO stroke, treatment decision-making can be complex whenever significant time has passed and brain tissue injury has already developed. The most recent EVT clinical trials have shown us that our current imaging biomarkers are unable to discriminate between patients who will benefit from intervention and those who will have poor outcomes or complications despite reperfusion. The Alberta Stroke Program Early CT Score (ASPECTS) and CT perfusion volumes remain imprecise and rudimentary tools, and we need a better way to triage patients in the emergency setting.

With the support of the TNS Grant, we have proposed this research project to personalize the imaging evaluation for patients with acute stroke using modern data science techniques. We have developed a novel approach to provide nuanced analysis of emergent non-contrast head CT (NCHCT), and we aim to validate this approach in a pilot study at two major stroke hubs in Texas. This algorithm performs automated NCHCT pre-processing and calculation of net water uptake (NWU) in each major region of the brain. NWU is an imaging marker that quantifies the degree of edema and tissue injury based on density differences between the stroke area and quantifies the degree of edema and tissue injury based on density differences between the stroke area and normal brain tissue. NWU has been shown to reliably predict the incidence of malignant cerebral edema after stroke utilizing commercially available software. We have developed our own approach to calculating NWU on NCHCT, and based on our preliminary data we hypothesize that NWU can accurately predict long-term patient outcomes and fill the current gap in standard stroke imaging evaluation.

We anticipate the immediate impact of this pilot study is the validation of a new stroke imaging marker that can provide a more nuanced evaluation for neurologists and neuro-interventionalists who are making treatment decisions for patients with LVO AIS. The treating physicians will be able to better select patients who will benefit from invasive intervention, and the added prognostic information can also support conversations with patients and families. Ultimately, the software could be implemented at stroke centers across Texas where patients are emergently evaluated for acute stroke in order to expedite stroke treatment times and maximize the likelihood of good functional outcome.

Project Goals:

Our primary aim is to validate an automated net water uptake algorithm for the prediction of 90-day functional outcome for patients with LVO undergoing EVT. The primary outcome with the predictive performance of this new imaging biomarker compared to standard ASPECTS and CT perfusion, quantified by area under the receiver-operating characteristic curve (AUROC).

Hypothesis: The NWU biomarker will be able to accurately predict the incidence of 90-day modified Rankin Scale (mRS) 0 to 2 after EVT based on initial NCHCT (AUROC>0.80), and the performance will be significantly better than standard ASPECTS and CTP.

Preliminary Results

Our research collaboration brings together two large stroke centers in Texas, UTHealth Houston and the Texas Stroke Institute (TSI) in Plano, TX. With the initial data collected so far, we have tested two preliminary research hypotheses. First, we wanted to determine whether this new CT biomarker, net water uptake, had a significant association with specific post-stroke neurological outcomes including language impairment and motor weakness. The prediction of patient-specific outcomes could eventually be impactful for acute stroke treatment decision-making and prognosis discussions. We collected, cleaned, and quality checked the cohort dataset which ultimately included 776 subjects. The CT images were then pre-processed, segmented, and analyzed using the existing algorithm that we previously developed. The resulting NWU values for each subject were than collated with the clinical dataset. To statistically test the association between NWU and the clinical outcomes, we used multivariable logistic regression so that we could include confounder variables that are commonly known to have an influence on patient outcomes. The resulting regression models showed excellent performance to predict whether or not subjects would have language impairment at the time of hospital discharge, with an area under the receiver operating characteristic curve (AUROC) of 0.851. The full results will be presented

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A Novel Approach to Expedite Acute Stroke Triage in Texas

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in an upcoming publication. The next step will be to meticulously collect the 90-day functional outcomes from the data records of each subject, so that we can evaluate the predictive performance of the new biomarkers with long-term stroke outcome.

A second hypothesis that we tested with the early dataset was focused on the subjects with the most severe stroke. Specifically, we included subjects with the large vessel occlusion and a large infarct core at the time of their initial presentation to the emergency department. These patients may benefit from emergent endovascular treatment, but existing triage tools for not reliable to guide decision-making. We evaluated whether the NWU biomarker would be able to reliably predict long-term functional outcome quantified by the 90-day modified Rankin Scale (mRS). After collecting and cleaning the clinical data as well as the NWU calculations from the CT image algorithm, we statistically tested the association with multivariable logistic regression. We found that higher NWU decreases the odds of having a good 90-day mRS for these subjects with severe stroke (Odds ration 0.74, 95% confidence interval 0.52-0.95). There were only 64 included subjects so a detailed analysis was not possible, but this TNS-supported project will allow us to build the cohort for full validation and external testing.

Future Directions

This proposed study would be the first to apply an open-source algorithm to calculate NWU and predict long-term patient outcomes after LVO stroke. If the hypothesis is true, it will demonstrate that advanced imaging and expensive software are not required to reliably triage patients with acute stroke in Texas. This approach could become a new way that we can start to bridge the gaps for Texans who live in neurologically underserved areas. After completion of this pilot study, we will plan to perform a prospective implementation study. Ultimately, this NWU-based approach to provide a more nuanced imaging evaluation compared to standard scores and could become a validated tool in the emergent setting to give personalized results to the treatment team. With this philosophy, we hope to maximize information from low-cost imaging, improve treatment efficiency and outcomes, and guide patients and families with stronger data.

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Exploring the Efficacy of Transcutaneous Electrical Nerve Stimulation (TENS) for Migraine Prevention in Chronic Migraine Patients

Miguel Elizarraras MS-2, Pankaj Satija, MD

Background

Migraine is a complex neurological condition marked by recurring moderate to severe headaches, often accompanied by nausea, vomiting, and sensitivity to light and sound (1). Chronic migraine is characterized by the occurrence of headaches for 15 or more days each month over a minimum period of three months, significantly impacting patients' quality of life and productivity (2). In the United States, migraines are the sixth most prevalent disease, affecting 18% of women and 6% of men. According to the Global Burden of Disease study 2016, migraines are now the second leading cause of disability among men and women across all age groups (3). They also impose a significant economic burden, with annual medical expenses ranging from $13 to $17 billion in the United States (4). Current guidelines from the American Headache Society recommend acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), beta-blockers, and triptans as effective treatments for migraines. However, current preventive therapies often have limited effectiveness and unpleasant side effects, resulting in suboptimal outcomes and substantial unmet medical needs. Furthermore, research found that merely 28% of patients experiencing episodic migraines and 45% with chronic migraines utilize preventative medication (5). As a result, there has been an increased demand for non-pharmacological treatment options.

Transcutaneous Electrical Nerve Stimulation (TENS) has emerged as a promising non-pharmacological intervention for pain management, though its effectiveness in preventing migraines remains unexplored (3). TENS involves applying low-voltage electrical currents through electrodes on the skin to modulate pain perception by stimulating sensory nerve fibers (6). Preliminary evidence indicates that TENS may influence pain pathways involved in migraine pathophysiology by modulating the activity of neurotransmitters including GABA, dopamine, and serotonin (4). The electrical modulation of neurotransmitters can alter the neuron's firing rate, thus modulating pain and frequency of migraines (7). This trial will explore TENS as a potential treatment option for migraine management.

Research Objectives

This trial seeks to evaluate the efficacy of transcutaneous electrical nerve stimulation (TENS) in managing chronic migraines. It will specifically assess its ability to reduce frequency, intensity, and duration of migraine episodes, which includes both acute and prophylactic benefits. Additionally, this trial will investigate the safety profile of TENS, with a specific focus on its tolerability, adverse effects, and overall treatment adherence.

Beyond symptomatic relief, the trial will aim to evaluate the impact of TENS therapy on patient's quality of life and medication usage. It will particularly focus on reductions in acute rescue medication use.

The study aims to provide robust data on the clinical utility of TENS as a treatment option for chronic migraine management.

Methods

50 patients diagnosed with chronic migraines according to the International Classification of Headache Disorders (ICHD-3) will be recruited for the study. Exclusion criteria include patients who have changed or started migraine prophylactic medication in the last 30 days

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and patients utilizing other neuromodulation devices (e.g., occipital nerve stimulation, vagus nerve stimulation). Prior to treatment, patients will undergo a screening process to determine the frequency, intensity, and duration of migraine episodes. Additionally, their medication usage and level of disability will be evaluated using the Migraine Disability Assessment (MIDAS).

The participants will be randomly assigned to active TENS therapy or sham TENS. Therapy consists of bilateral stimulation of supraorbital nerves for 20 minutes, 5 times weekly, for 12 weeks. Active TENS therapy is 10 Hz with a pulse width of 100 µs while sham therapy consists of 2 Hz, 100 µs pulse width. The initial therapy session will take place in the clinic, during which patients will receive comprehensive instructions on proper device usage and be monitored for any potential adverse effects. Each participant will then be provided with a TENS device along with detailed instructions. Patients will also receive a migraine calendar to systematically document TENS therapy usage, including the frequency, duration, and intensity of migraine episodes, as well as medication use. Participants will be systematically evaluated at 4-week intervals to monitor progress, adherence, and potential adverse effects. At these visits, patients will complete a MIDAS assessment to track changes in migraine-related disability and review migraine calendars to assess therapy compliance, migraine frequency, duration, intensity, and medication usage. Once the intervention phase concludes, the study team will analyze the data to determine the efficacy, safety, and tolerability of TENS therapy for migraine prevention in chronic migraine patients.

Current Status and Progress
We are currently in the recruitment and screening phase of the project and have identified 45 patients who have met the eligibility criteria. We anticipate completing the recruitment and screening process by the end of the year and aim to start the trial in January 2025.

Challenges and Updates
We have encountered delays in receiving the TENS units due to logistical issues with our supplier. However, we expect the shipment to arrive within the next month. Once received, we will prioritize distribution to participants and initiate therapy sessions promptly to minimize any impact on the study timeline.

Next Steps
Following the completion of the recruitment and screening phase, participants will be randomly assigned to active TENS therapy or sham TENS therapy and will promptly being the active trial phase. Once participants are equipped with TENS devices and provided with migraine calendars, they will start their at-home therapy sessions. Active TENS or sham treatments will be administered as per the protocol - 20-minute bilateral stimulation of the supraorbital nerves, 5 times weekly, for 12 weeks. Patients will be re-evaluated at 4-week intervals. Data collection from these assessments will be ongoing throughout the 12-week therapy period.

Expected Outcomes/ Further Directions
The trial is expected to demonstrate a significant reduction in migraine frequency, duration, and intensity following TENS therapy. It is also expected to improve quality of life and reduce medication usage.

Research has shown that current pharmacological preventive therapies often have limited effectiveness and come with high costs and wide range of side effects. If proven effective, transcutaneous electrical nerve stimulation (TENS) therapy could offer a safe, non-pharmacological option for the management of chronic migraines. This has the potential to reduce the burden on chronic migraine patients, who are often limited by medication side effects and treatment options. Additionally, this study may enhance our understanding the migraine pathophysiology, including neural and pain modulation mechanisms, and support the development of new therapeutic approaches.

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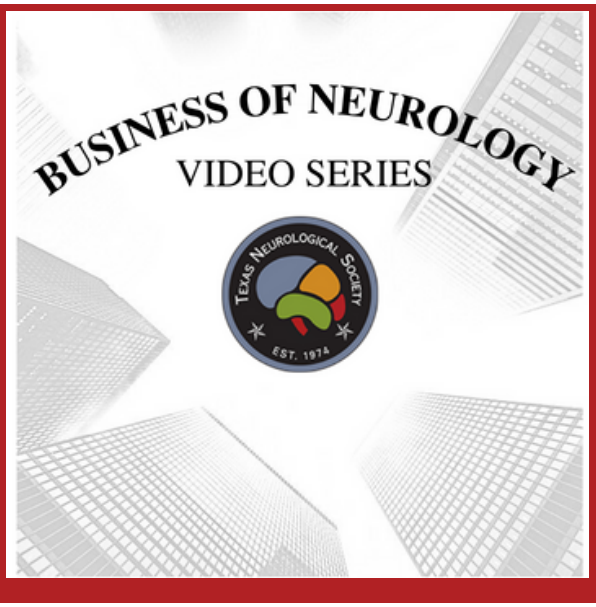

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New Look, Same Trusted Academy: AAN Launches Brand Update

A visually refreshed website. An updated look and tone. A redesigned logo, including a new take on the classic neuron symbol. These are all part of the AAN's first brand update in 25 years - an exciting change that reflects the organization's thriving neurology community.

"Earlier this year, we announced an updated mission statement: To enhance member satisfaction and to promote brain health for all," said AAN President Carlayne E. Jackson, MD, FAAN. "Our worldwide AAN community is made up of the leaders, innovators, and champions in neurology. We want our brand to reflect our mission and our members, who are at the center of the brain health conversation."

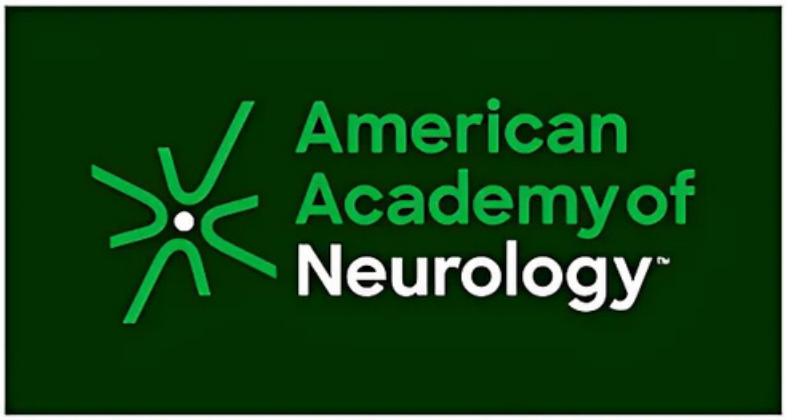
The mission update was announced along with the AANs first five-year strategic plan, which laid out organizational values as well as a set of crucial goals. By the end of 2028, the AAN aims to grow a diverse neurology workforce, strengthen neurological practice, promote neuroscience research, and improve neurological health.

The changes, which were developed through invaluable member insight and feedback, highlighted another need: A fresh, modern presentation that honors both the AAN's legacy and its future. The Board of Directors, which is comprise entirely of AAN members, took the opportunity to explore a refreshed look that works on all digital platforms as the growing Academy connects with members - and anyone who's curious about brain health - around the world.

While the updated brand is a modern take on past visuals, it takes care to honor AAN history: The neuron, formerly depicted as a gold start, takes on a versatile and dynamic shape. And of course, Academy green - the color that shows up in hundreds of outfits at the Annual Meeting, on neckties for Neurology on the Hill, and in all kinds of AAN programs and products - takes center stage.

After all, while the new look helps highlight the AAN's place at the center of brain health, it's still the same Academy that has served members for more than 75 years.

"Our vision, as always, is to be indispensable to our members," Jackson said. "We will always be your world-class hub for education, science, practice tools, and conference - and we're looking forward to another 75 years and beyond."



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