

Perinatal and Childhood Stroke: Emergent Management and Emerging Therapies

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Disclosures

No financial disclosures

I will be discussing off label use of thrombolysis and endovascular clot retrieval in children

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UTHealth Houston Department of Pediatrics, Division of Child Neurology

UTHealth Institute for Stroke and Cerebrovascular Disease

NIH Child Neurologist Career Development Program K12 Award

Objectives

1. Define the presentation of perinatal and childhood stroke
2. Discuss the most important initial steps in emergency diagnosis and management of childhood and perinatal stroke
3. Review outcomes and long-term management of childhood and perinatal stroke survivors



Visit www.iapediatricstroke.org for information

A Bit About Adult Learners (That's You!)

Andragogy – The Art and Science of Helping Adults Learn by Malcolm Knowles (1980):

- Need to know WHY we should be learning
- Need internal motivation
- Want to know how learning will help SPECIFICALLY
- Bring prior knowledge and assumptions as their foundation
- They are self-directed and want to take charge
- They find relevance from task-oriented learning

To start

I will answer your two most burning questions:

- Q: Do kids have strokes?
 - A: Yes
- Q: Dr. Fraser, are you old enough to be teaching us this?
 - A: Yes.
 - I'm older than I look.



Who's this guy talking to us?

- **Past Training:**
 - General Pediatrics
 - Neurology with Special Qualifications in Child Neurology
 - Vascular Neurology
 - So now I see kids and adults with stroke in Houston, Texas.

Pediatric Stroke Program

Pediatric Stroke Program Quick Links:

- [What Is A Pediatric Stroke and What Are Potential Causes?](#)
- [Research and Clinical Trials](#)
- [Publications](#)
- [Pediatric Stroke Clinic](#)
- [UTHealth Houston Pediatrics](#)
- [In The News](#)

Who Are We?

At UTHealth's Pediatric Stroke Program, we provide clinical care and conduct research related to pediatric stroke and cerebrovascular diseases. Pediatric stroke is an underrecognized medical emergency, among the top 10 causes of morbidity and mortality in the pediatric population. Currently, there is a shortage of pediatric neurologist specifically trained in diagnosis, acute management and long-term care of pediatric patients with cerebrovascular diseases. Our pediatric stroke program works closely with our partners at [Children's Memorial Hermann Hospital](#) to provide comprehensive medical care to children and families affected by pediatric stroke and cerebrovascular diseases.

Mission Statement

Our mission is to provide pediatric stroke patients with compassionate, comprehensive, and personalized care. We strive to support our patients by creating a nurturing and inclusive community for children with cerebrovascular disease. We are committed to performing innovative, cutting-edge research to continuously advance stroke care for young stroke survivors.

Meet Our Pediatric Stroke Team



Melika Abrahams, RN, BSN, CPN
Cerebrovascular Nurse, Pediatric Stroke Program

Department of Pediatrics |
Division of Child & Adolescent
Neurology
UTHealth Houston



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Case #1

HPI:

A 12 hour old term infant ('Layla') develops seizures and encephalopathy at about 12 hours of life.

What are the chances it's a stroke?

Neonatal Seizures:

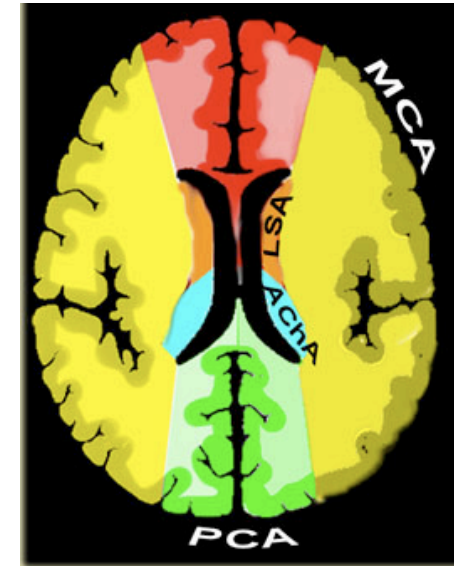
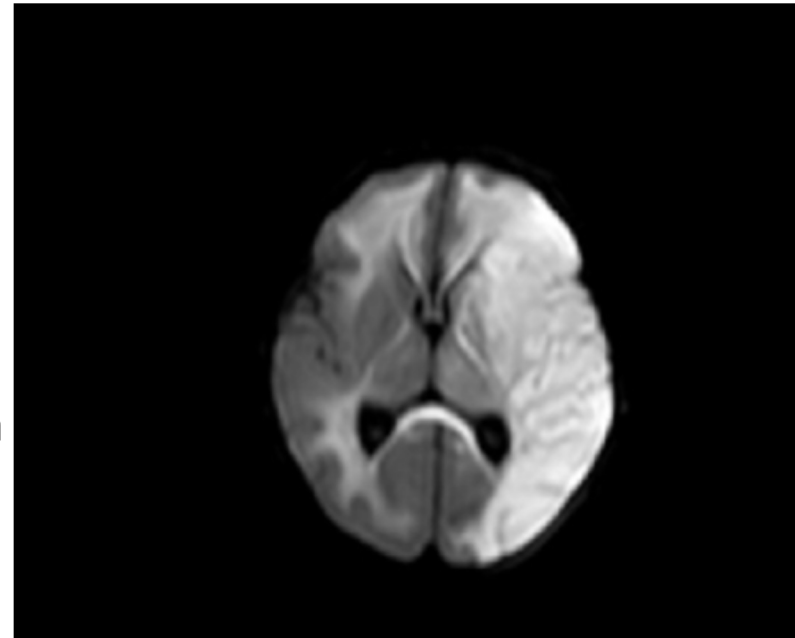
1. Hypoxic Ischemic Encephalopathy (60%)
2. Stroke (almost 20%!)
3. Some other neonatal brain injury
4. Hypoglycemia/electrolyte abnormalities
5. Something else (like genetic disorders, etc)

Case #1

HPI:

A 12 hour old term infant ('Layla') develops generalized seizures and encephalopathy at about 12 hours of life.

MRI is obtained demonstrating the findings on the right.



Let's Define 'Stroke'

Injury (across all groups)

- Arterial Ischemic Stroke (55%)
 - Blood can't get in
- Intracerebral Hemorrhage (40%)
 - Blood where it's not supposed to be
- Cerebral Venous Sinus Thrombosis (5%)
 - Blood can't get out

Age

- Perinatal
 - 28 weeks gestation to 28 days of extrauterine life
 - Incidence – take a guess
 - 1 in **1,100**
- Childhood
 - 29 days of life to 18 years of life
 - Incidence? Take a guess
 - 1 in 25,000 children **per year**

Acute Perinatal Arterial Ischemic Stroke Management

ABCs (duh!)

Control Seizures!

- Transfer to a NICU

Workup (per AHA scientific statement 2019)

- MR Angiogram of the brain and neck, MR Venogram of the brain and neck
- Echocardiogram
- DIC screen
- Not much else!

Acute Care?

- Supportive

In children with normal cardiac anatomy and perinatal stroke, incidence of childhood stroke is the same as children without perinatal stroke

Pathophysiology

Arterial Ischemic Stroke

- Usually unknown
- Though to be related to placental factors
- Associated with 'precipitous birth'
 - Low APGARS, Nuchal Cord, need for intubation, etc.

Periventricular Infarction

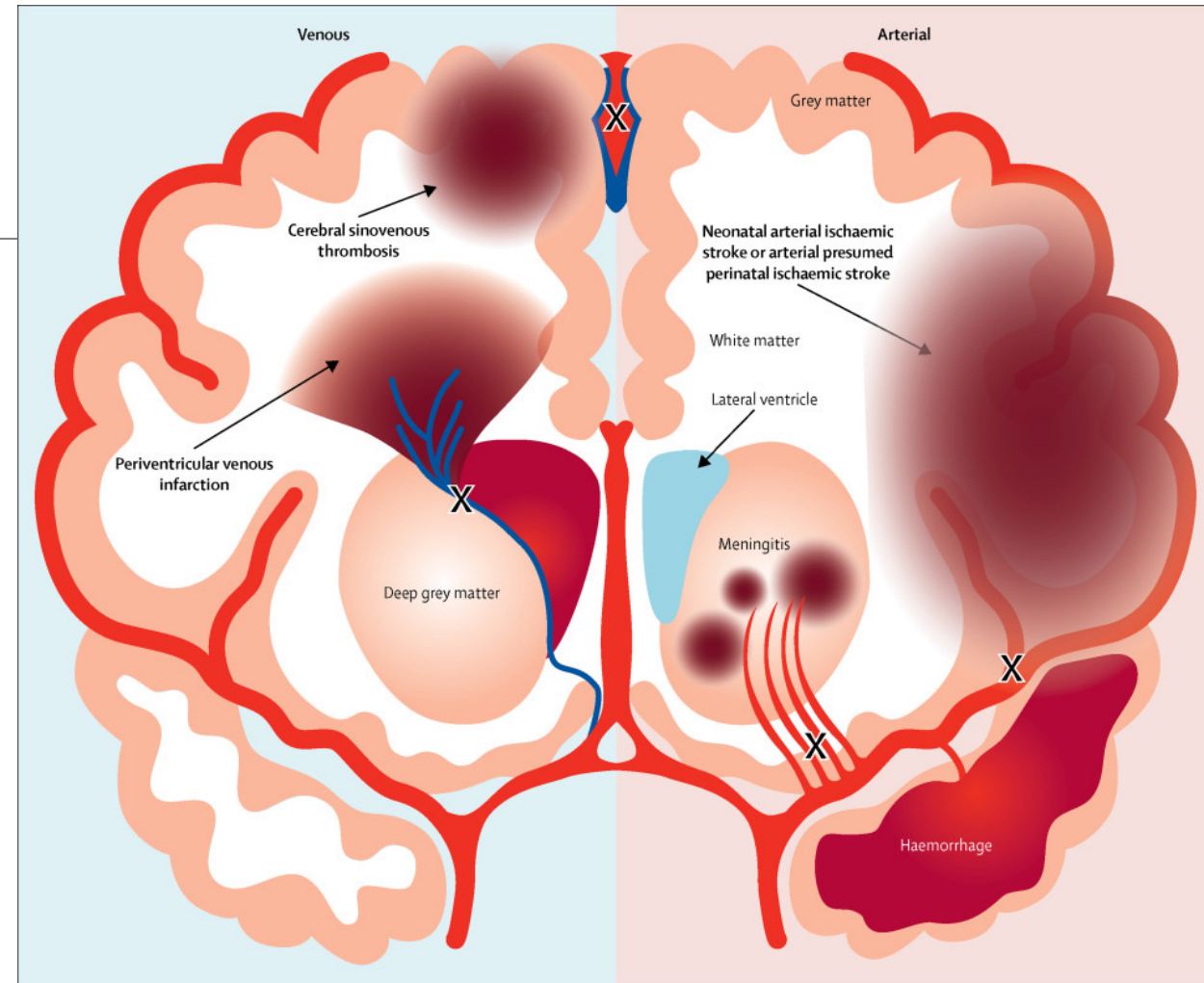
- Usually due to IVH causing impaired venous outflow

ICH

- Likely related to birth trauma

CSV

- Can be precipitated by dehydration and infection, and often not treated with anticoagulation



Outcomes

Stroke is the most common cause of hemiplegic cerebral palsy

Pathologic early handedness typically starts around 6 months

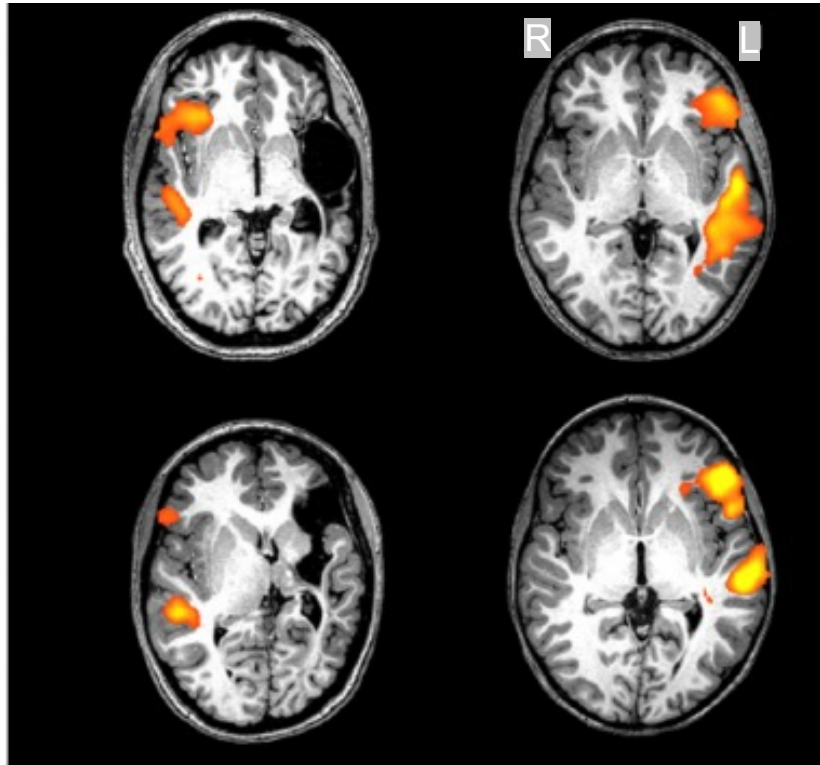
Some patients will have 'normal' motor development, some will have cerebral palsy

Normal language by adolescence, but lower IQs than siblings

Epilepsy – **10-20% (so most DON'T have epilepsy).**



Children Can 'Migrate' Language



But there are limits!

(and rules)

You start to **lose** the ability to migrate language to the other side at about 5-6 years of age

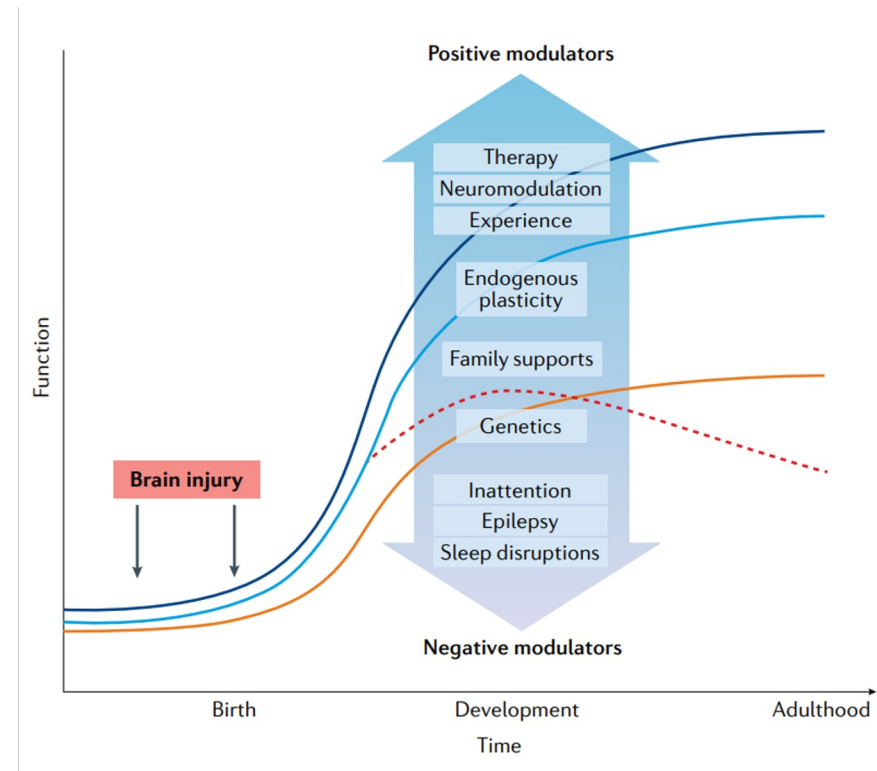
Functionally lose that plasticity by about 13 years

Neonatal Stroke Outcomes

Each child is different, and every patient has their own potential

In adults, recovery is defined by *regaining lost function*

In children, it is perhaps better to define recovery by *achieving developmental milestones*

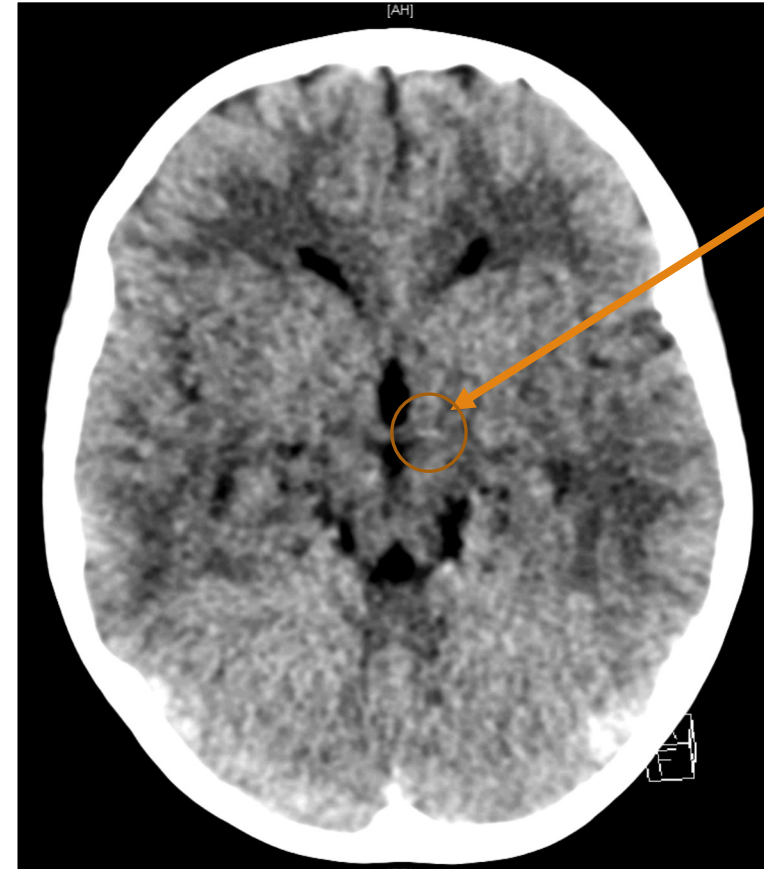


Part 2: Childhood Stroke

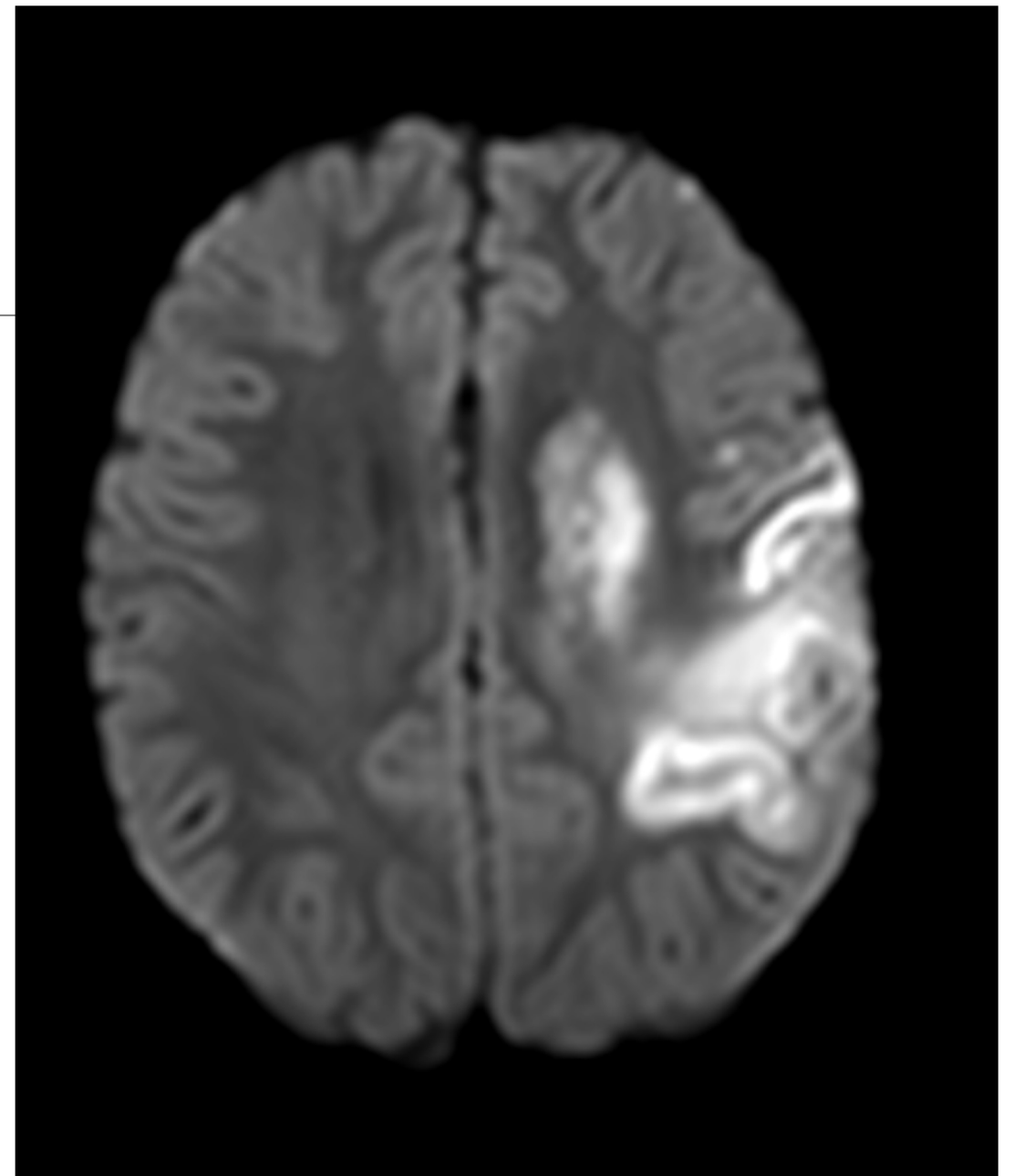
Case #2

A 6 year old girl with congenital heart disease is brought to the ED by EMS at 6:00PM after having sudden difficulty walking at 5:30PM. A CT Brain at 9:00PM is normal. She is admitted for observation.

A routine consult to pediatric cardiology is called in the morning. The cardiology attending sees the patient at 10:00 AM and notices right facial droop and arm weakness. An emergent MRI is ordered at about 10:30 AM and pediatric neurology is consulted.



In AM cardiology attending notices weakness and calls a code stroke

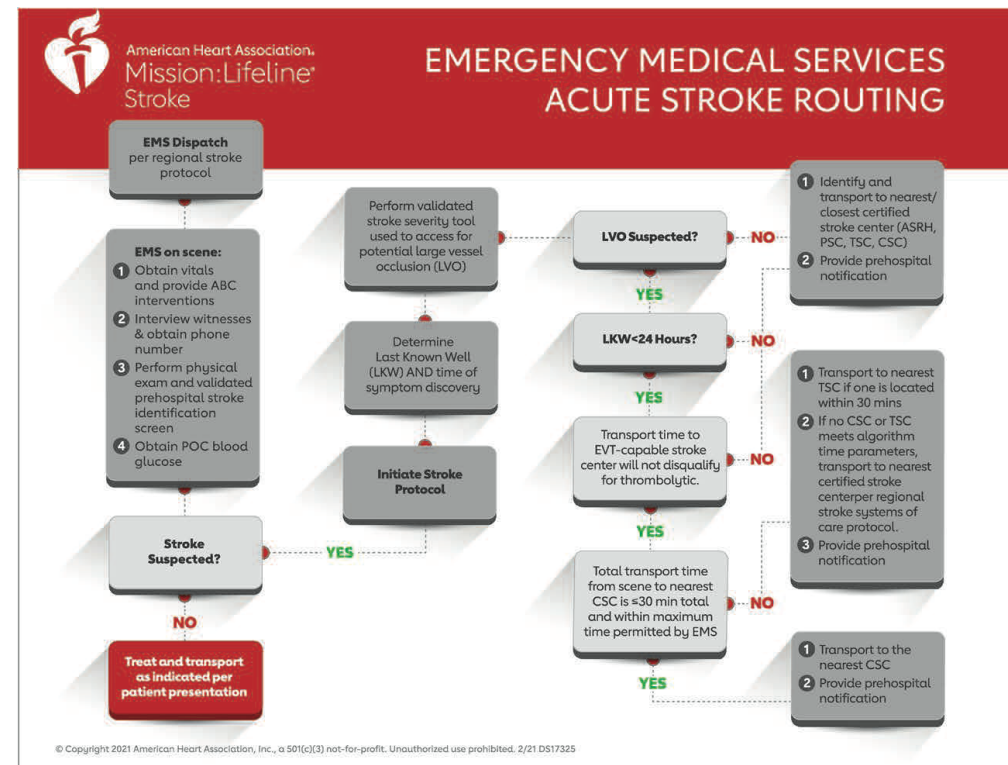


Case #3 – 15 year old with weakness

A 15 year boy “Alex” with no medical history collapses on the football field at 4:30PM. EMS arrives at 4:45PM after being called by coaching staff. On arrival he is awake, speaking, but doesn’t move his left arm, has a left facial droop, and his eyes are looking to the right.

Differential?
Seizure
Stroke
Toxic/Metabolic

What do we do?



Let's assess the evidence...continued

- Pediatric stroke is among the **TOP 10 most common cause of death in children**
 - **Seriously. Number 9 on the list.**

- About **40% are hemorrhagic and 60% are ischemic** in pediatric patients
 - Hemorrhage is most commonly caused by vascular malformations (40-80%), then coagulopathy (10-20%)
 - Cerebral Venous Sinus Thrombosis incidence is 0.5/100,000/year

But what about for this 6 year old with weakness?

Once in a while a child in your care will concern you for an acute stroke. They might present with:

Lateralized weakness ~50-75%

Speech difficulties (aphasia or dysarthria) ~ 50%

Unilateral or mixed sensory loss ~25-50%

Dyscoordination (ataxia) ~ 25%

Sudden Cranial Nerve deficits ~10%

Seizure ~ 25%

Non-specific altered mental status ~ 25-50%

Sudden unexplained headache especially with altered mental status – (THINK HEMORRHAGE!)

KNOW THE SIGNS OF A STROKE WITH BEFAST

Immediate treatment of a stroke is vital to minimize the longterm effects of stroke and prevent death.

With each passing second during a stroke, brain cells are dying, so remember that time is brain!



5th

Stroke is the 5th leading cause of death in America and a leading cause of adult disability.

**795,000
Americans**

Approximately 795,000 Americans suffer a stroke each year.

**4
minutes**

Someone dies from a stroke every 4 minutes.

**40
seconds**

A stroke occurs every 40 seconds.

**80
percent**

Up to 80% of strokes can be prevented with a healthy lifestyle.

Balance

Loss of balance or unsteadiness



Eyes

Blurred vision



Face

One side of face is drooping



Arms

Weakness in arms or legs



Speech

Trouble with speech

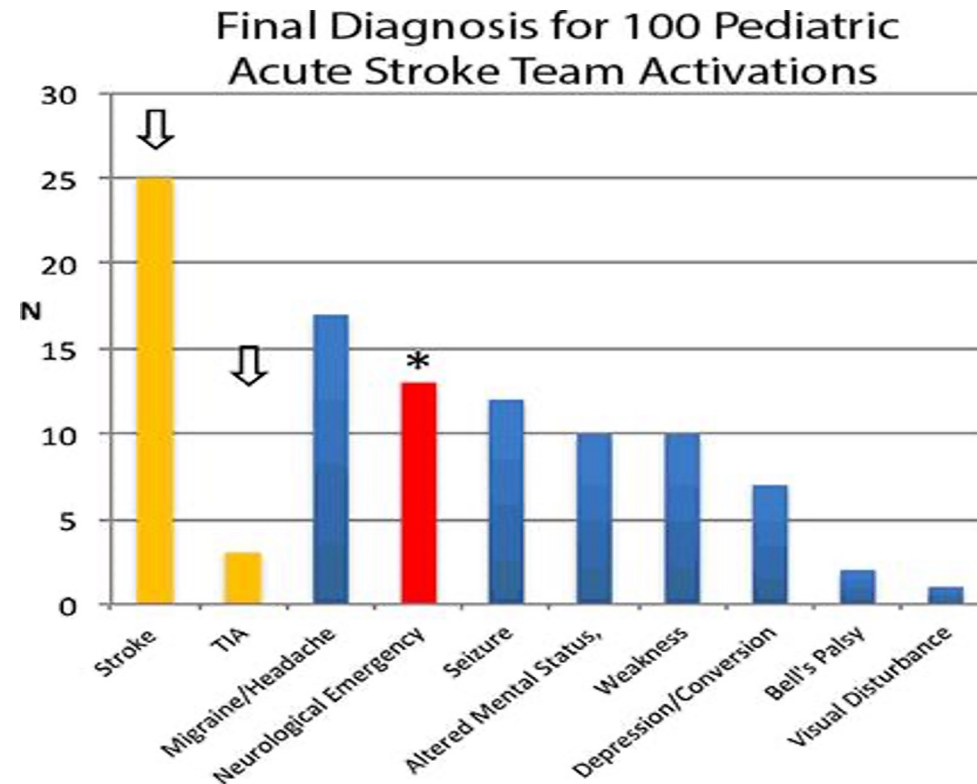


Time

Call 9-1-1!

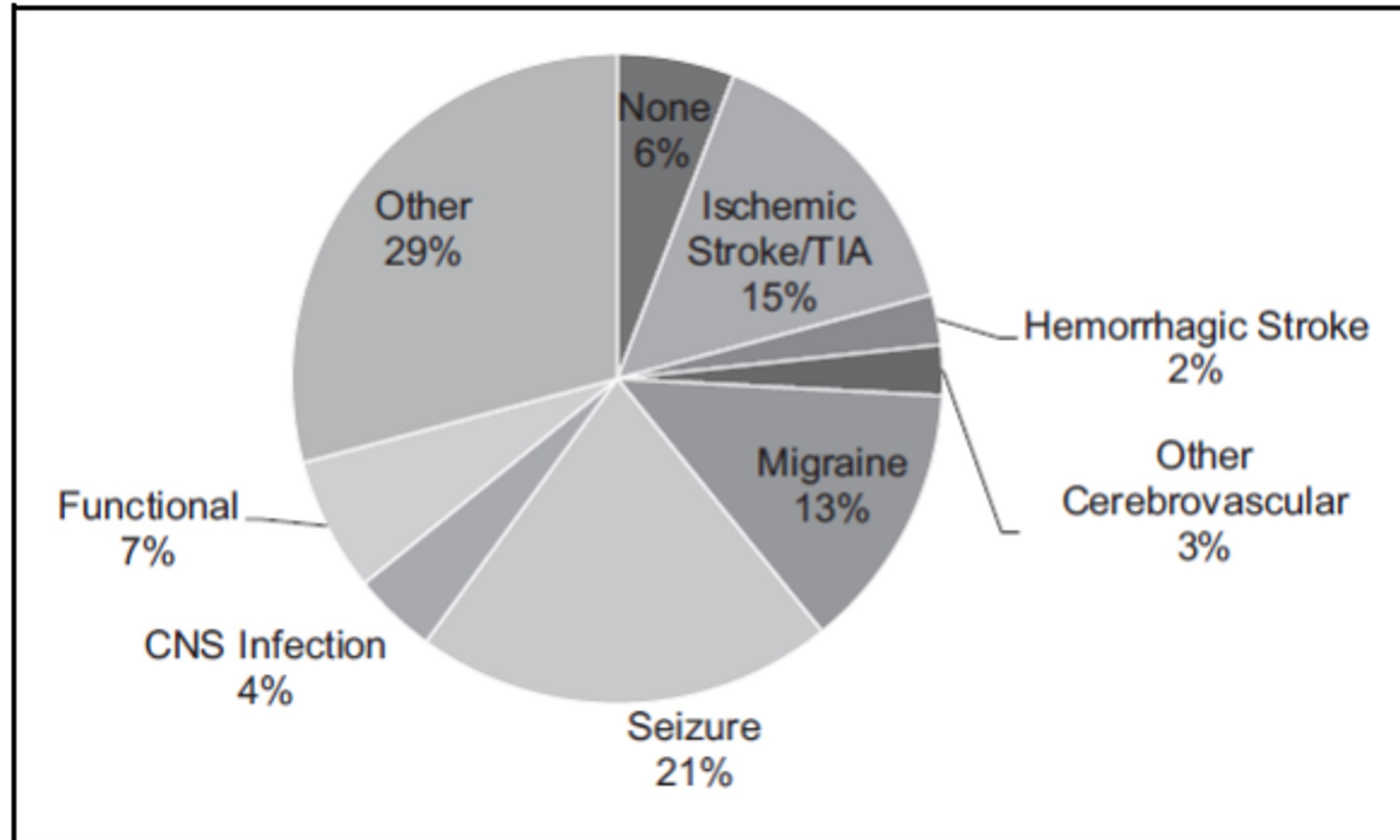


European Stroke Group

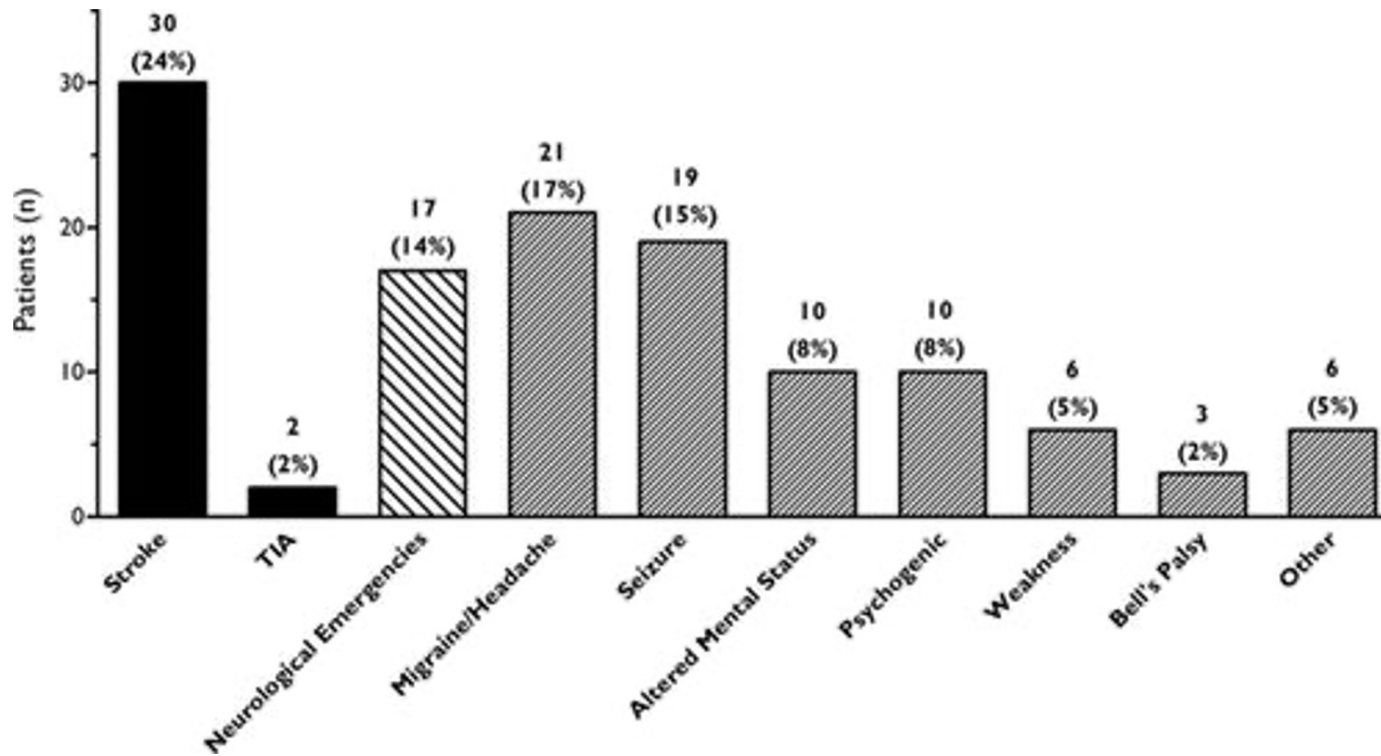


*Neurological emergencies include: neoplasm 3, viral meningitis 4, bacterial meningitis 1, demyelinating disorder 1, hydrocephalus/shunt malfunction 1, hypertension 1, methotrexate toxicity 1, and head trauma/shear injury 1

Johns Hopkins



Monroe Children's Hospital (Vanderbilt)

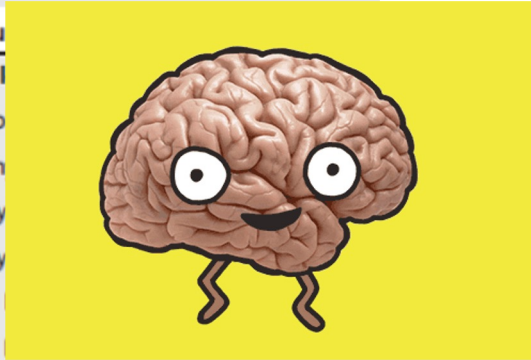


Pedi Ischemic Stroke Risk Factors

TABLE 8-2 Risk Factors and Comorbidities for Stroke in Children and Young Adults^a

Pediatric^b

Young Adult^c



Well
To
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Dy



Atrial fibrillation 2%

Continued on page 161

TABLE 8-2 Risk Factors and Comorbidities for Stroke in Children and Young Adults^a *Continued from page 160*

Pediatric^b

Young Adult^c

Potentially Modifiable Risk Factors

High-risk alcohol consumption	33%
Migraine, lifetime history	27%
Sleep ≤ 6 hours per night	18%
Obstructive sleep apnea	3%

PEDIATRIC VERSION OF THE RACE SCALE:
THE PED-RACE SCALE



N=50 children
Pediatric Stroke Code
in Catalonia (Spain)

Pediatric RACE Scale
Facial palsy
Arm motor function
Leg motor function
Head and eye deviation
Aphasia or agnosia
TOTAL SCORE 0-9

1 Ped-RACE (EMS or ED)

2 Ped-RACE + Ped-NIHSS (child neurologist)

**Interrater agreement
Ped-RACE**

Cohen's Weighted Kapa 0.92

Ped-RACE score in:

AIS with LVO	6.5 [6-7]
AIS without LVO	0 [0-3]
ICH	2 [1-6]
Mimic stroke	1 [0-2]

**Correlation
Ped-RACE & Ped-NIHSS**
Spearman's rho 0.852

Easy to perform

Can be used by non-neurologists

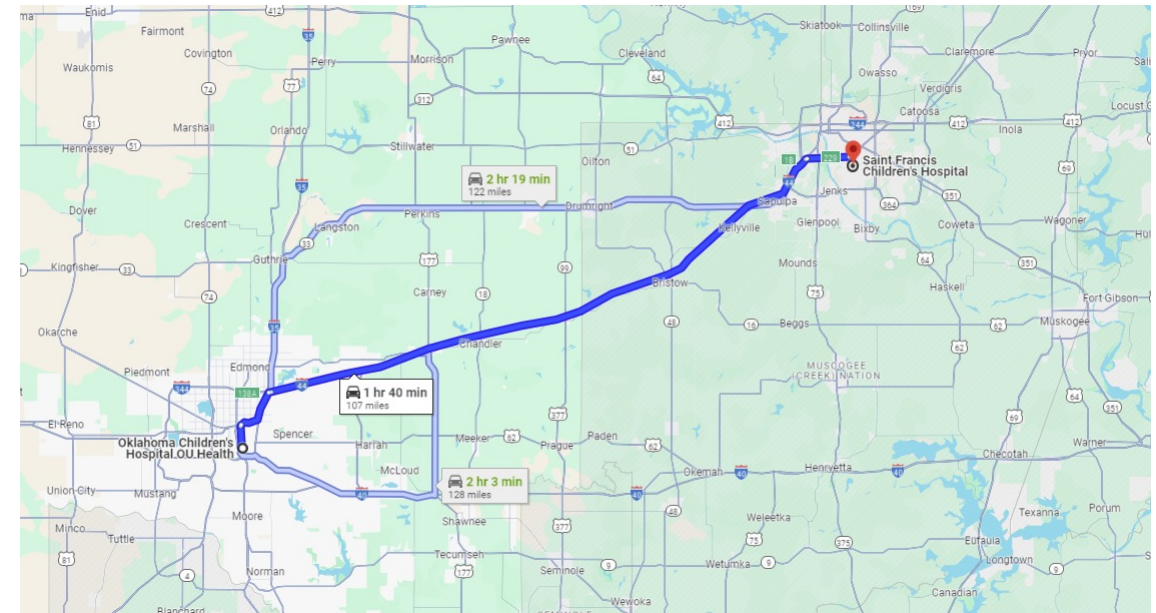
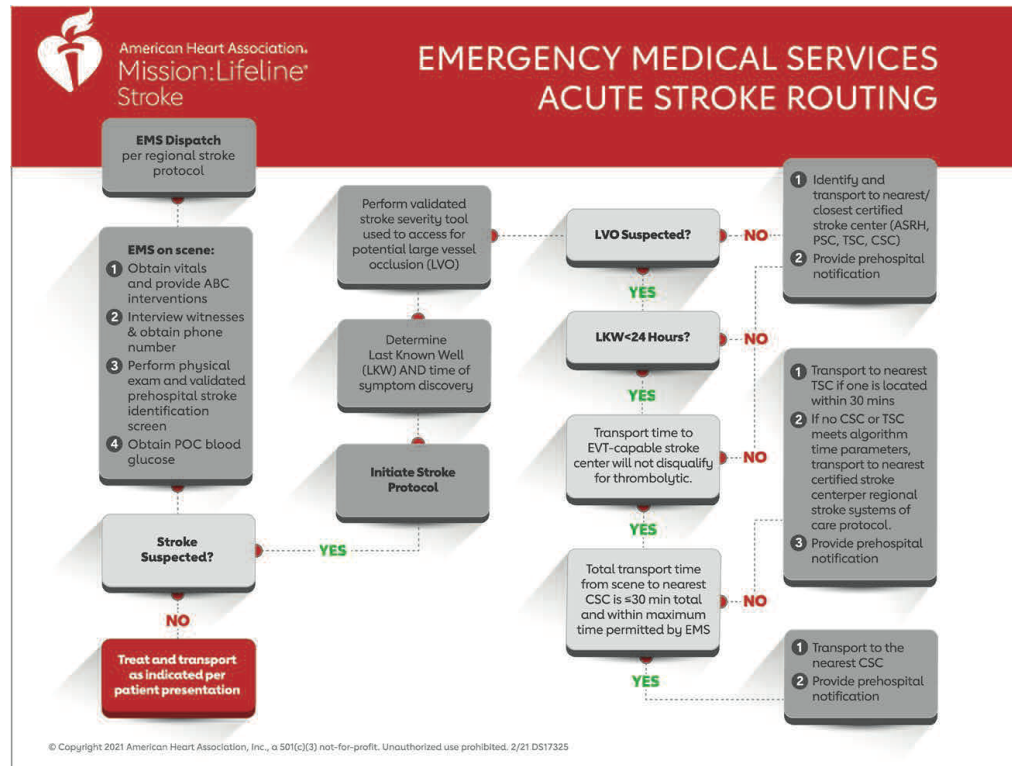
Identify LVO and more severe stroke children

Table 1. PedRACE Scale

Items	Adults and children >6 y	Children 2-6 y	Score
Facial palsy	Show teeth	Ditto	Absent: 0 Mild: 1 Moderate/severe: 2
Arm motor function	Raise and hold arms	Ditto	Absent/mild (>10 s): 0 Moderate (<10 s): 1 Severe (unable): 2
Leg motor function	Raise and hold legs	Ditto	Absent/mild (>10 s): 0 Moderate (<10 s): 1 Severe (unable): 2
Head and gaze deviation	Observation	Ditto	Absent: 0 Present: 1
Aphasia (right hemiparesis)	"Close your eyes" "Make a fist"	"Where is mom/dad?" "Touch your nose"	Both tasks correctly: 0 1 task correctly: 1 Neither task correctly: 2
Agnosia (left hemiparesis)	"Whose arm is this?" "Can you lift both arms and clap?"	"Whose arm is this?" "Where is the hidden toy?"	Both tasks correctly: 0 1 task correctly: 1 Neither task correctly: 2

So where do we transport him

In the adult world you would do this:



- In the pedi world, you can go to one of the two places in Oklahoma that can handle cases of suspected pediatric stroke:
1. Saint Francis (they have a code stroke and thrombectomy pathway)
 2. Oklahoma Childrens (they have a code stroke and thrombectomy pathway)

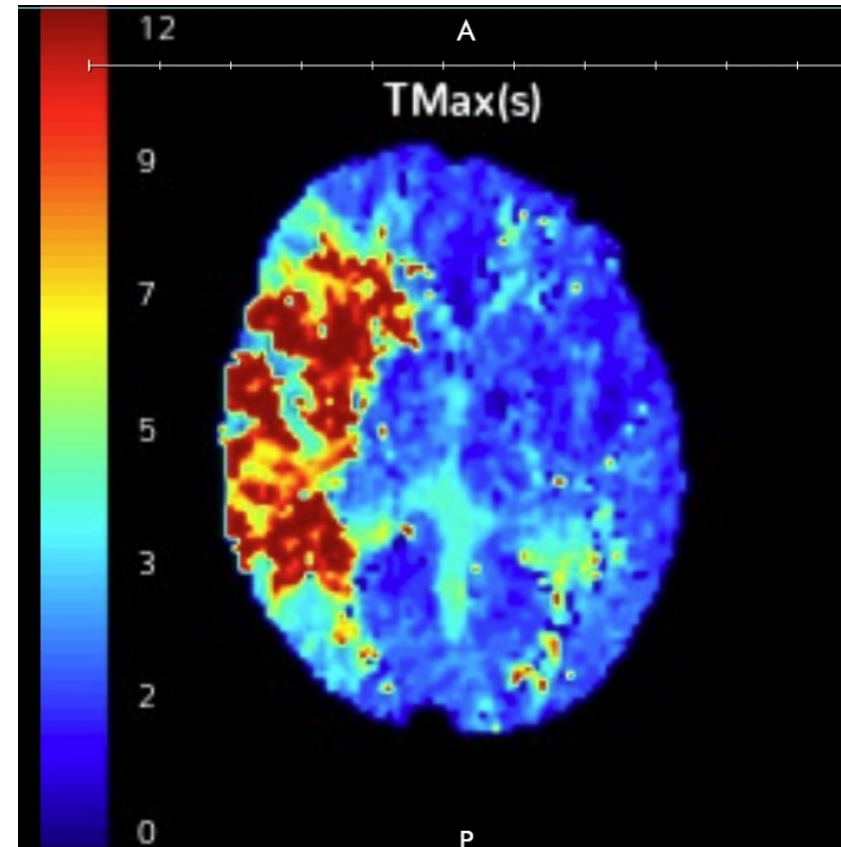
Case #3 (continued)

You know that kids can have strokes. You transport him straight to Saint Francis and pre-call it in as a possible stroke

On arrival, he appears weak on the left side, and is becoming drowsy

The PEDNIHSS certified ER nurse calculates a PedNIHSS score of 10 and a stat CT/CTA/P is done.

Where's the problem?



Thrombolysis? Thrombectomy?

Thrombolysis – the use of a ‘clot buster drug’ administered IV, to attempt to lyse a symptomatic clot (TNK or tPA)

Thrombectomy – mechanical removal of a clot using an intra-arterial catheter

These are the main hyperacute treatments in ischemic stroke!

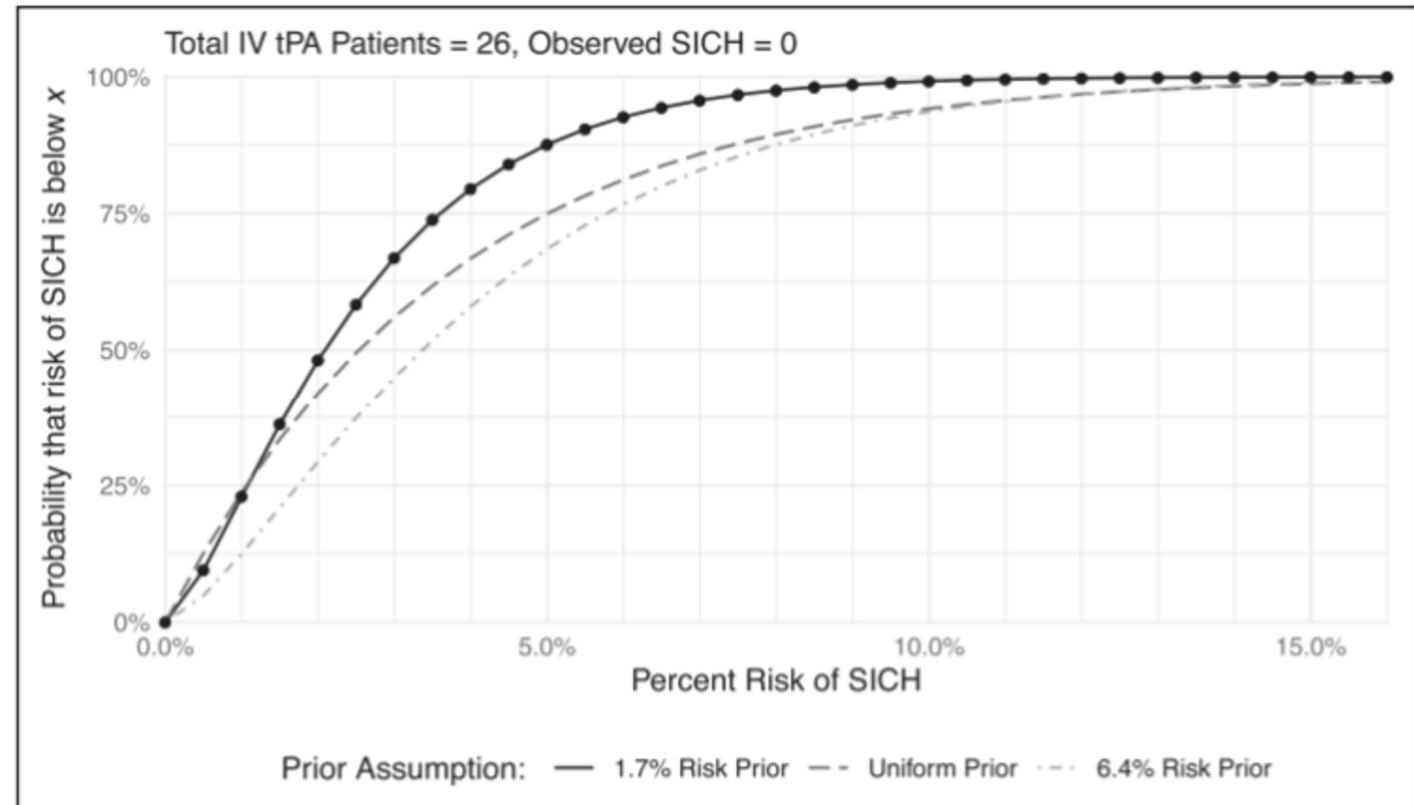
Thrombolysis is probably as safe in kids as it is in adults (IF USED CORRECTLY)

It is dangerous and potentially FATAL if given to a child incorrectly

Data from the TIPSTERS extended observational study in children over 10 years revealed:

45 children received tPA

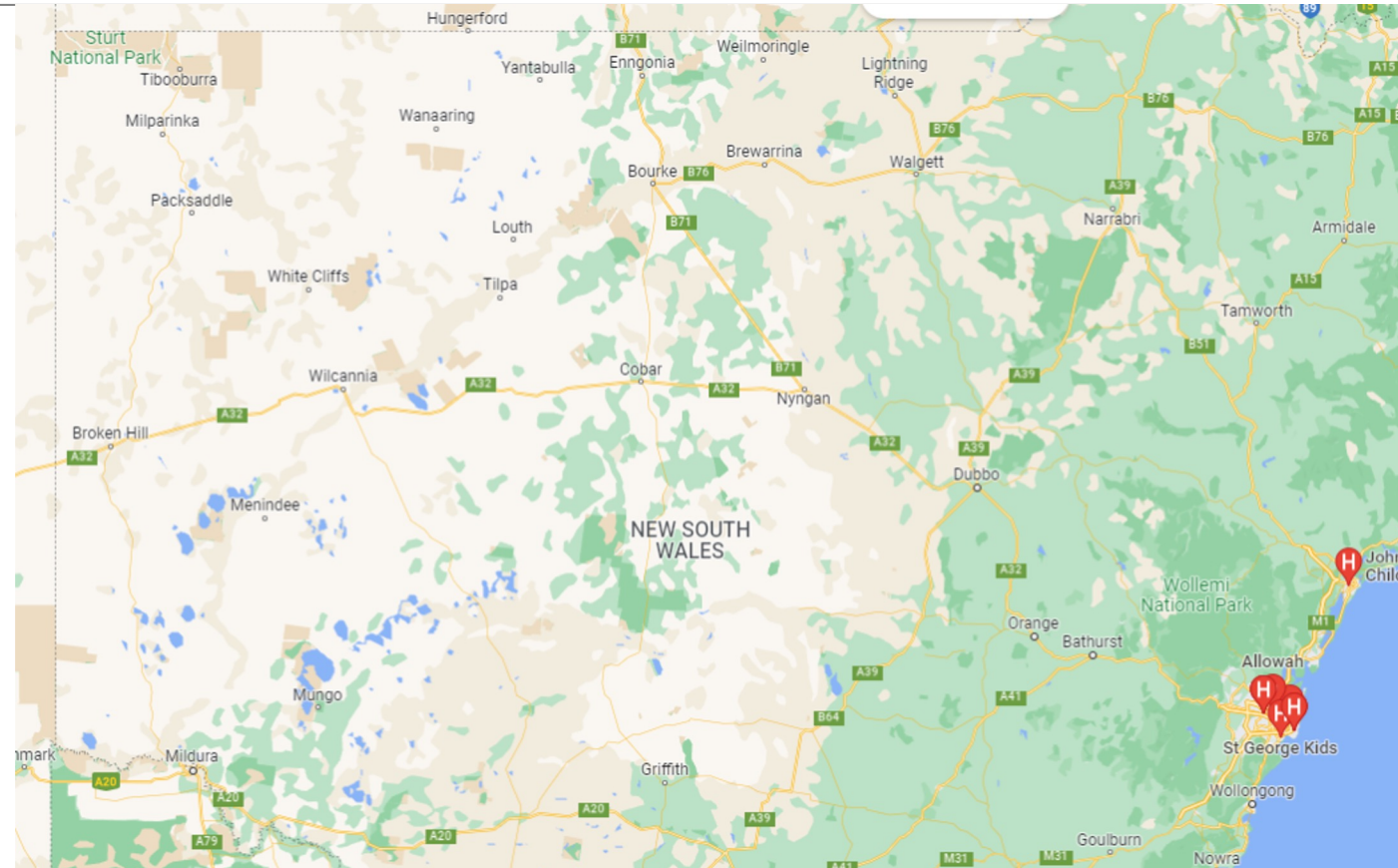
2 petechial hemorrhages on follow up imaging



Large Vessel Occlusion in Children: Registry from Australia

The authors obtained IRB approval from their institutions.

Design: Multicenter retrospective cohort study, aged 30 days to 16 years with acute AIS in this specific region of Australia from January 1st 2010 to December 31st 2019.



Large Vessel Occlusion (LVO) and Children

Table 3. Clinical Outcomes at 3 Months After Stroke (Primary Outcome)

Outcomes	No. (%)					OR (95% CI)	P value
	AIS	Non-LVO	LVO				
Dichotomous analysis ^c			All	No thrombectomy	Thrombectomy		
ped-mRS score	NA	NA	NA	NA	NA		
0-2	87 (53.0)	74 (58.7)	13 (34.2)	7 (26.9)	6 (50.0)	χ^2 , 8.803	.01
3-6	77 (47.0)	52 (41.2)	25 (65.8)	19 (73.1)	6 (50.0)		
0-2 (anterior circulation)	NA	NA	11 (33.3)	6 (25.0)	5 (55.6)	NA	NA
3-6 (anterior circulation)	NA	NA	22 (66.7)	18 (75.0)	4 (44.4)		

Take Home: Children who had the clot removed did better than children who did not

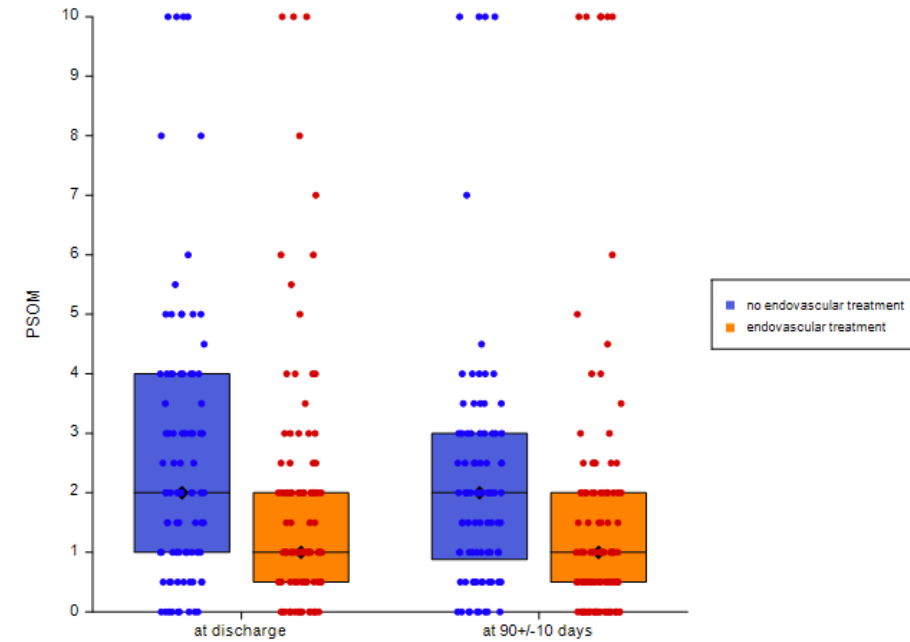
Just accepted

Endovascular Thrombectomy or Best Medical Treatment for Childhood Stroke - A Prospective Multicenter Registry (Save ChildS Pro)

Peter B. Sporns, MD, MHBA^{1,2,3}, Kartik Bhatia, MD^{4,5}, Todd Abruzzo, MD^{6,7}, Lisa Pabst, MD⁸, Stuart Fraser, MD⁹, Melissa G. Chung, MD¹⁰, Warren Lo, MD¹¹, Ahmed Othman, MD¹², Sebastian Steinmetz,

Figure 3

Title: Pediatric Stroke Outcome Measure at Discharge and Day 90 Post-stroke



Legend: Values in boxplots are median and interquartile range. Dots are single patients in total range.

Pediatric Acute Stroke Protocol

Note:
 Patients with known MELAS have a separate protocol for stroke-like episodes

For patients with MELAS presenting with focal neurologic deficits, **page pediatric neurology and see MELAS protocol**

Child 0-17 years old with concern for acute stroke

Patient meets **BOTH acute stroke criteria:**

1. There is a focal neurologic deficit
 - a. Unilateral weakness or sensory change
 - b. Painless vision loss
 - c. Dysarthria or aphasia
 - d. Nystagmus or ataxia
2. The problem has been present for 24 hours or less

No

Page Pediatric Neurology

The Pediatric Neurology team will see the patient and consult Dr. Stuart Fraser (or, if he is unavailable, the adult stroke team) if indicated

Note:
 Consider activating rapid response if patient is on wards to facilitate IV placement and rapid transport to imaging



Yes

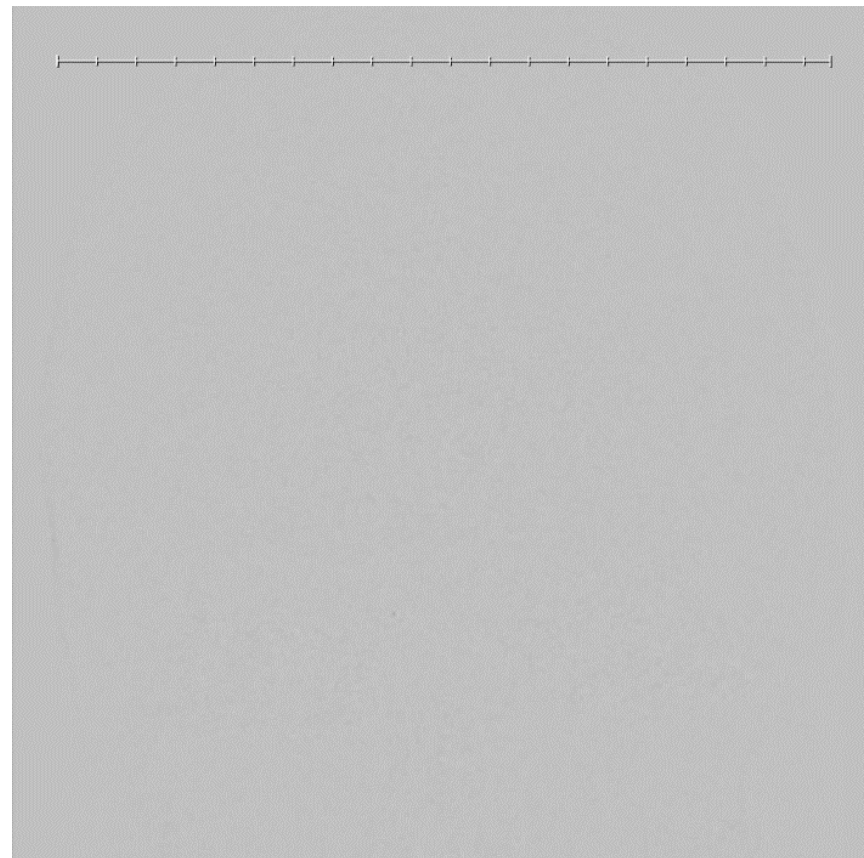
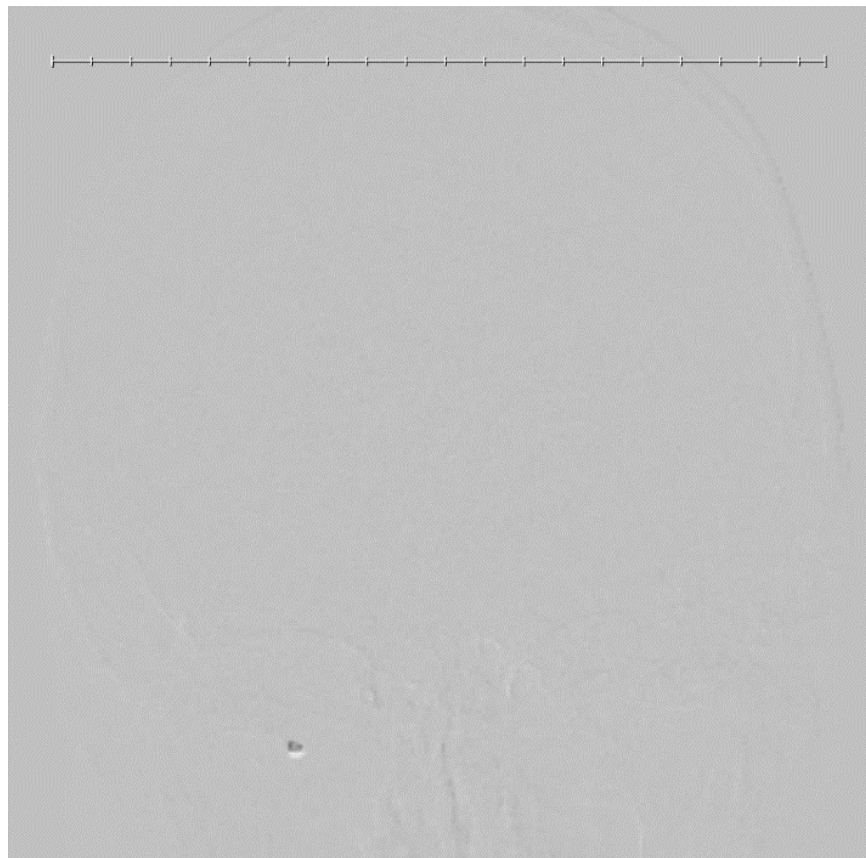
ED or Responsible Service:

1. Call the page operator and ask to page **Pedi Code Stroke**, the patient's location, and call back number
2. Start IV x2 (one dedicated IV for tPA)
3. Draw Stat CBC, BMP, PT/PTT/INR, Glucose
4. Initiate Neuroprotective care:
 - a. Normotension (between 50th-15% above the 95th %ile for age)
 - b. Normoglycemia, Normothermia, Normovolemia
 - c. Seizure Control. Stat AED if suspected Seizure
5. Bedside nurse completes MRI screening form STAT
6. Order and prepare patient for transport for **MRI Brain Stroke Limited + MRA Brain wo contrast +/- MRA neck wo contrast**



Go to Page 2

Case



And 2 years later?

1 rep max, Deadlift, 435 lbs

(He has joined the '1000lb' club)

Next steps? USMC.



Case # 4

A 15 year old boy (Kevin) with ADHD presents with 48 hours of headache, followed by 1 hour of lethargy and confusion

He requires an EVD which is eventually removed, and angiography confirms an arteriovenous malformation in his thalamus and occipital lobe.

Most (>80%) childhood spontaneous intracerebral hemorrhages are due to vessel malformations, most commonly arteriovenous malformations.



So...now what?

Varies patient to patient

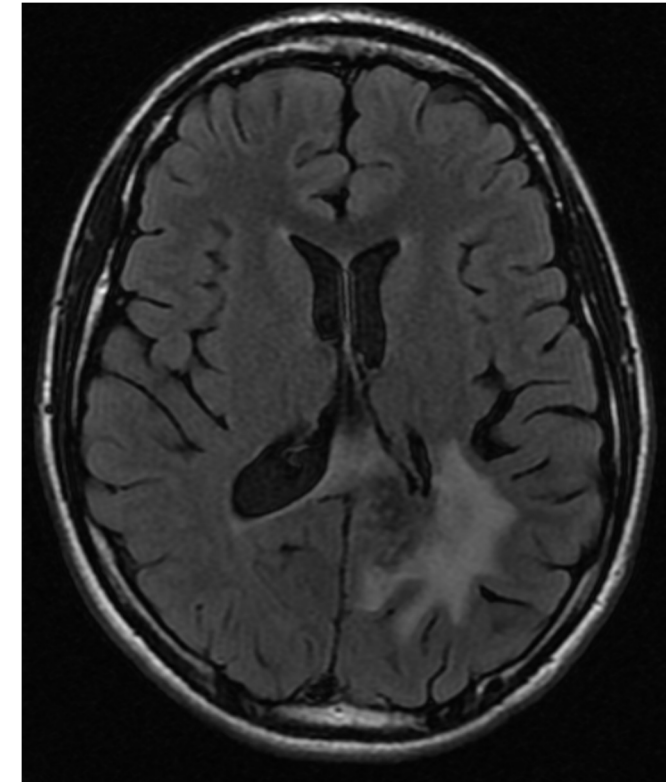
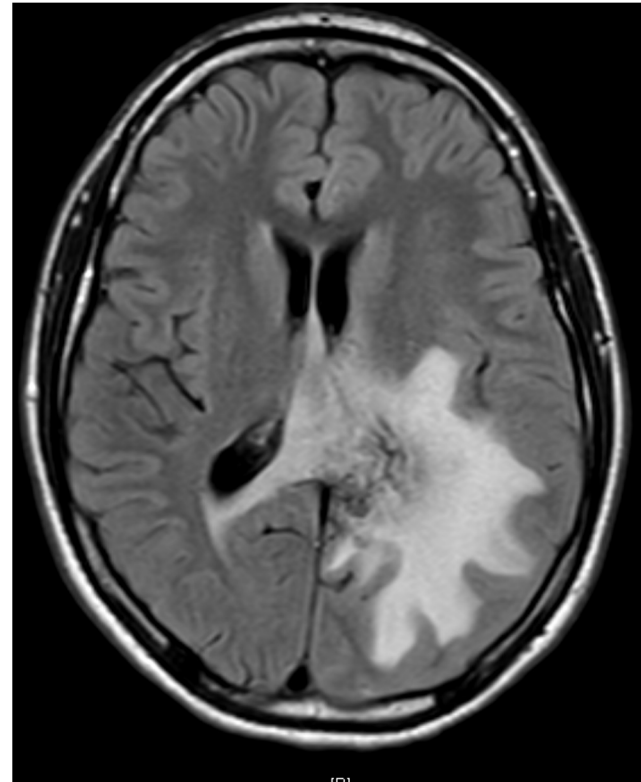
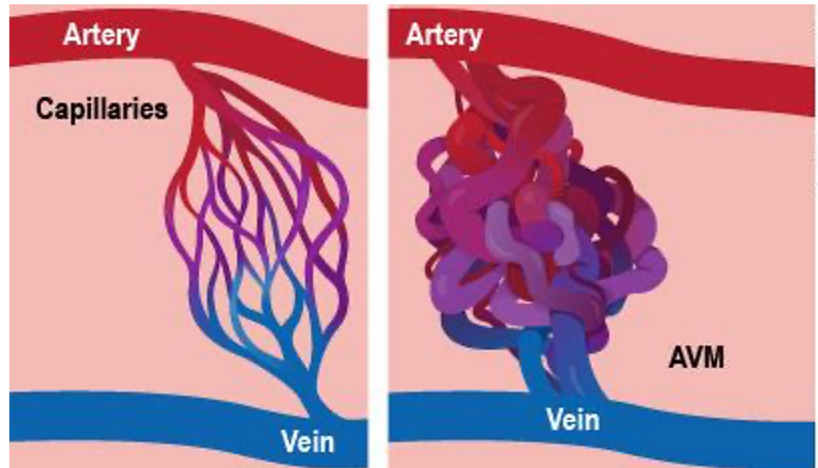
Options Include

- Surgery

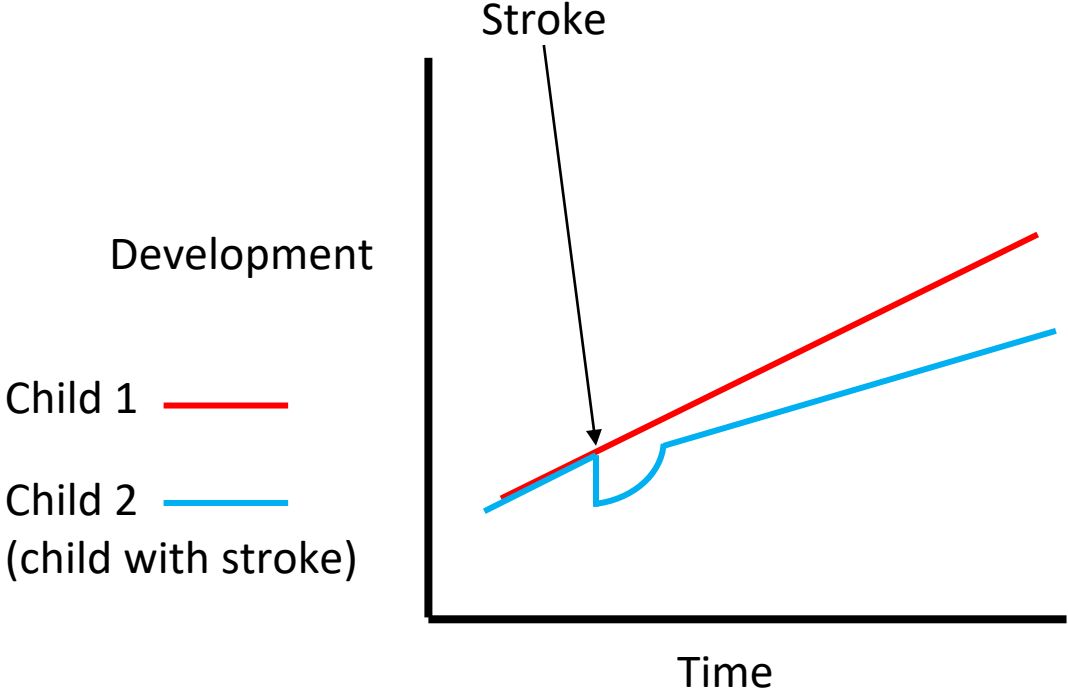
- Endovascular Embolization

- Gamma Knife Radiosurgery

- Or some combination of the above



Life After Pediatric Stroke

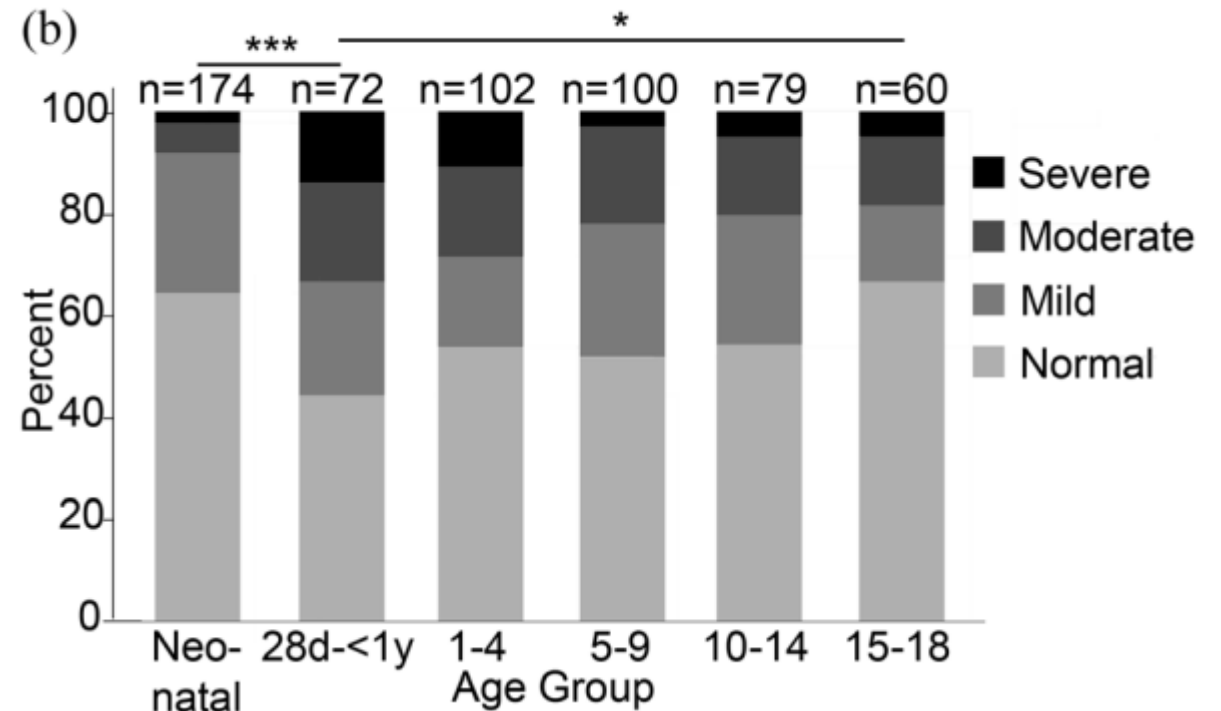


Models of Plasticity

Generally, younger patients are thought to have greater rehabilitation potential due to increased neuroplasticity

There are exceptions

Data from the International Pediatric Stroke Study in 2020 found younger age at stroke was associated with worse long term outcome



How can we help?

Models of rehabilitation:

1) Intensive

(several hours per day) – useful for breaking bad habits and initial recovery but not sustainable long term

2) Outpatient maintenance

A few hours per week. Typical of neonatal stroke and developmental delay in the USA

New Horizons

Multiple modalities in the future to investigate neuro-recovery and protection:

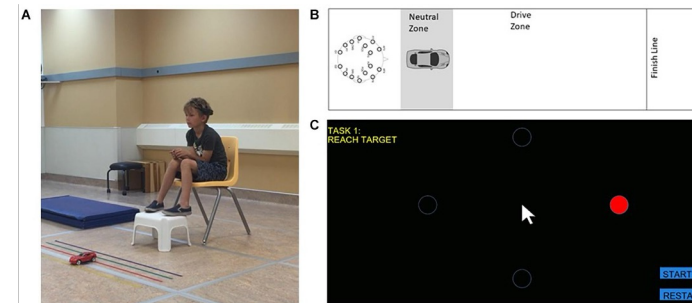
Transcranial stimulation (magnetic/direct current)?



Vagal Nerve Stimulation?

Vagus nerve stimulation paired with rehabilitation for upper limb motor function after ischaemic stroke (VNS-REHAB): a randomised, blinded, pivotal, device trial

Brain-Machine Interface?



tDCS



Figure 1 – Child in our lab wearing tDCS Device

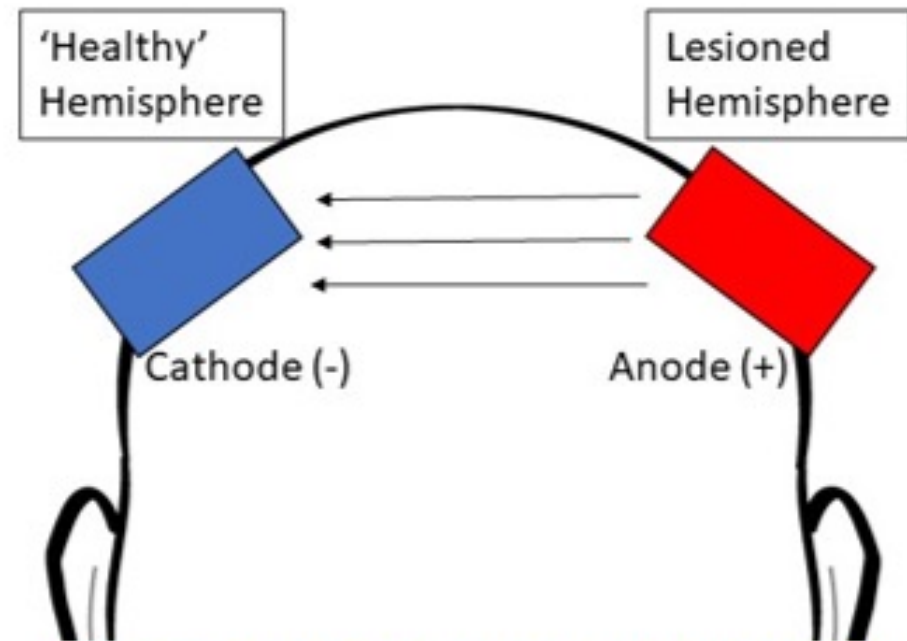


Figure 2 – Simple Schematic of Bihemispheric tDCS

Take Home

We (all) are taking care of patients with stroke

Children do NOT recover 'better' than adults!

Children with stroke suffer lifelong disability, some of which may not be obvious on the surface

Questions?

Email – pedistroke@uth.tmc.edu

To refer patients, ask questions, inquire about resources/research

Cell phone – call me anytime: 512-963-0438

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