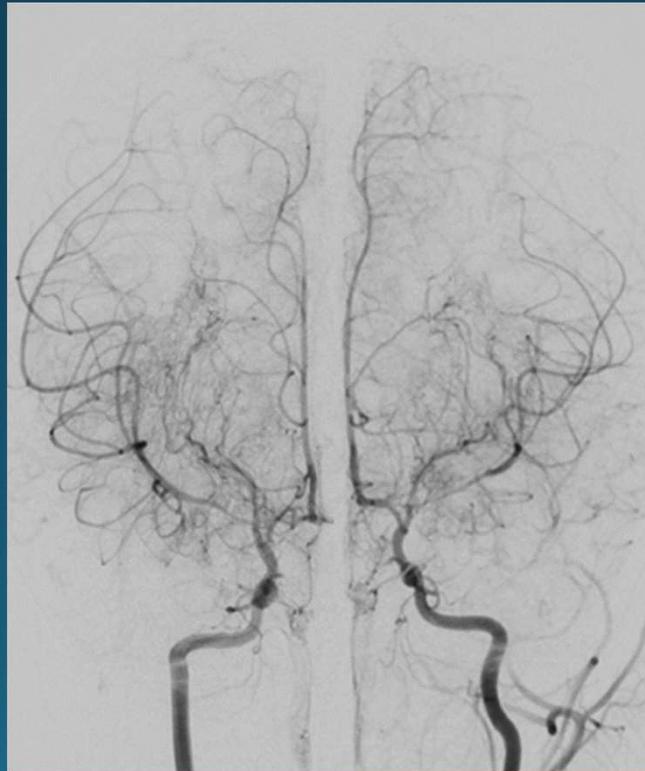
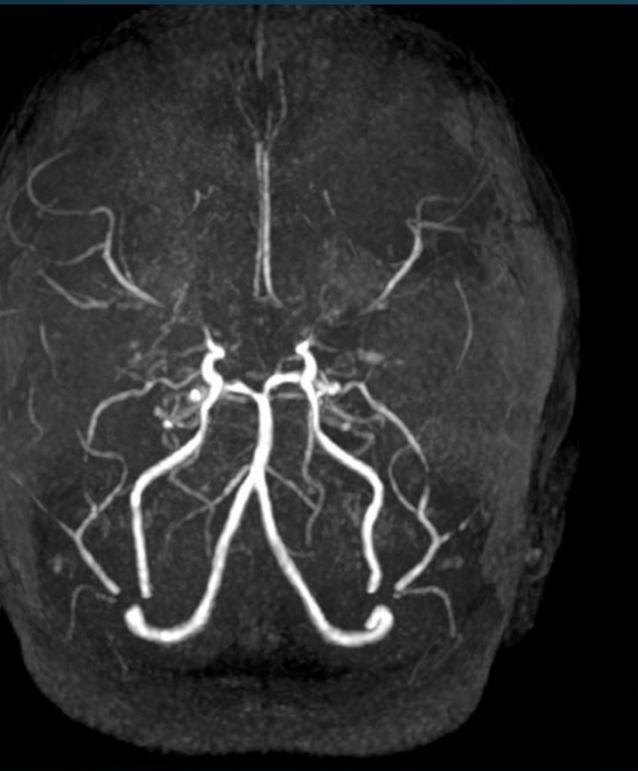


# Clinical manifestations of moyamoya disease: seizure in moyamoya disease



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# Things to say about...

- Concepts
- *Clinical manifestations*: Ischemic vs collateral-related
- Neuroimaging & treatment
- *Seizure in moyamoya disease*
- Take-home messages

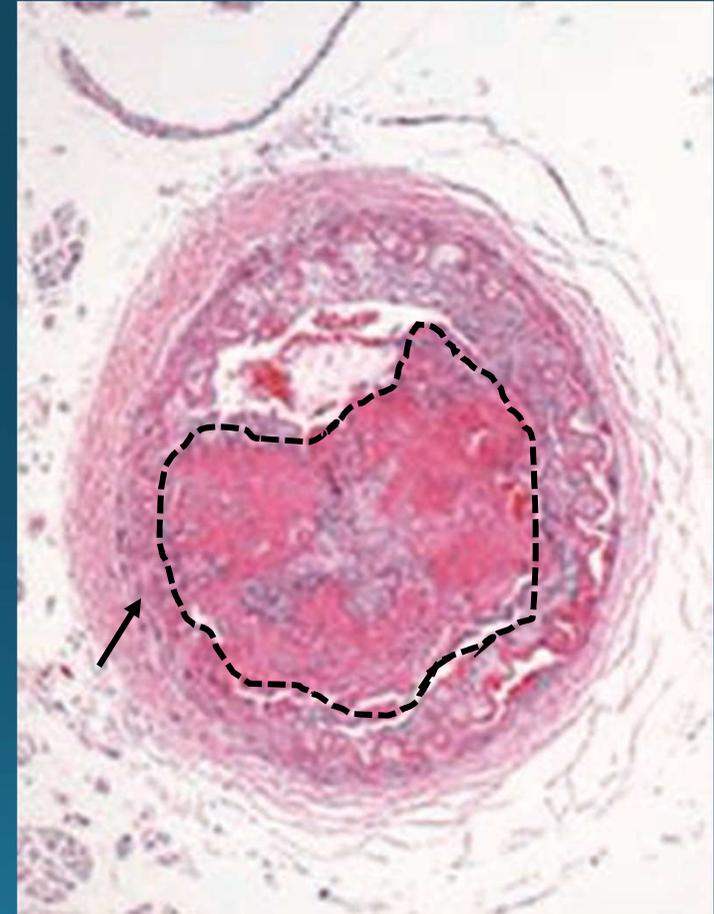
# Concepts

# Introduction

- Concept of moyamoya disease (MMD)
  - *Idiopathic* arteriopathy characterized by progressive occlusion of *bilateral*, distal ICAs *plus* compensatory collateral vessels (ie, basal collaterals = “puff of smoke”)
    - 2 age peaks: **5-8 y (ischemic stroke)** & 4<sup>th</sup> decade (hemorrhage)
    - Female predominance (M:F ratio = 1:1.8)
    - **Early diagnosis!**: with revascularization, stroke risk 80% → 4%

# Introduction

- Pathophysiology of the arteriopathy
  - Hyperplasia of smooth m. cells *plus* luminal thrombosis
  - No atherosclerosis or vasculitis
- In Japan & Korea: major sources of the patients
  - **Most common & treatable** cause of childhood ischemic stroke
  - *RNF213* polymorphism: in 80%-90%, early & severe form



# Confusing terminology

Terms	Meaning	Also known as...
Moyamoya disease	Primary (idiopathic) <i>plus</i> bilateral	Aka, “definite MMD” Common in Japan/Korea
Moyamoya syndrome	Secondary (Down’s syndrome, neurofibromatosis type I, sickle cell disease, supracellar irradiation, etc) <i>or</i> unilateral	Aka, “quasi-MMD” Common in western countries
Just “moyamoya”	Characteristic angiographic findings, regardless of causes	NA

# Disease progression

ICA stenosis ( $\pm$  ACA & MCA)



Basal collaterals  $\uparrow$



“Puff of smoke”



ECA-pial collaterals  $\uparrow$



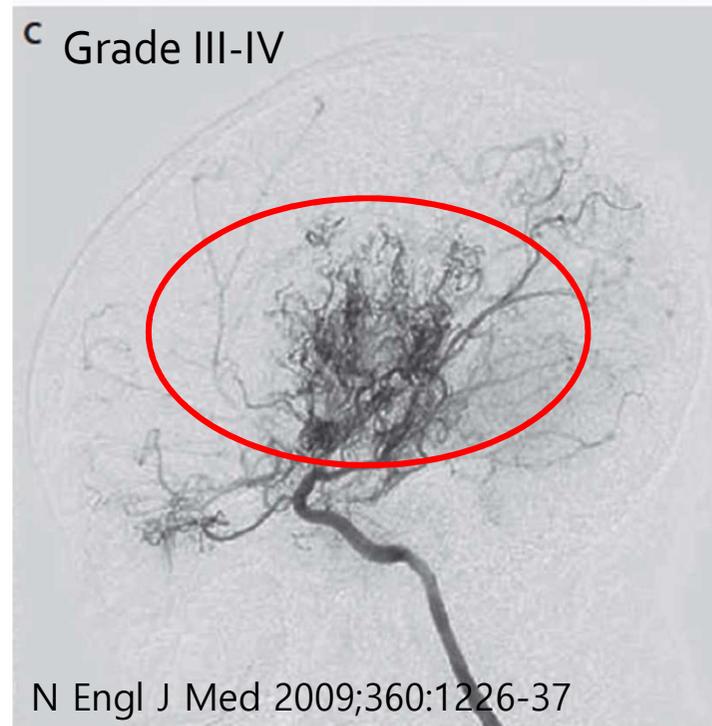
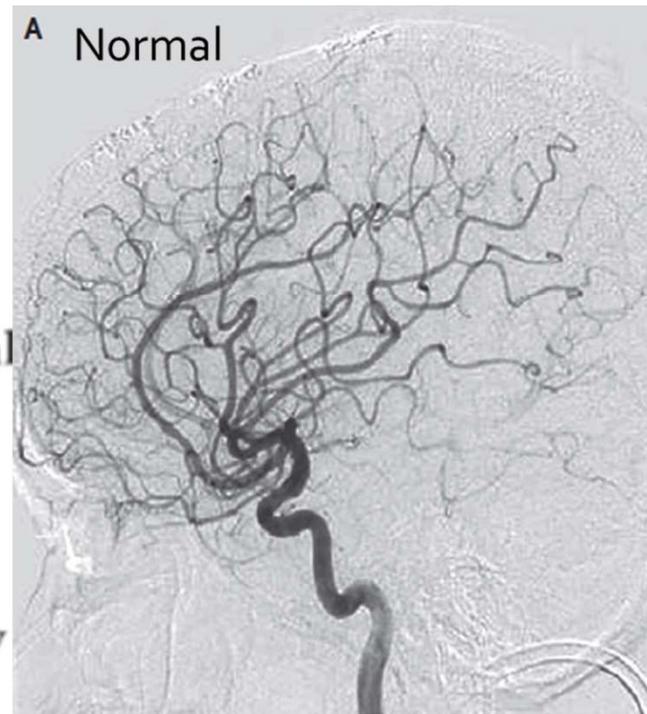
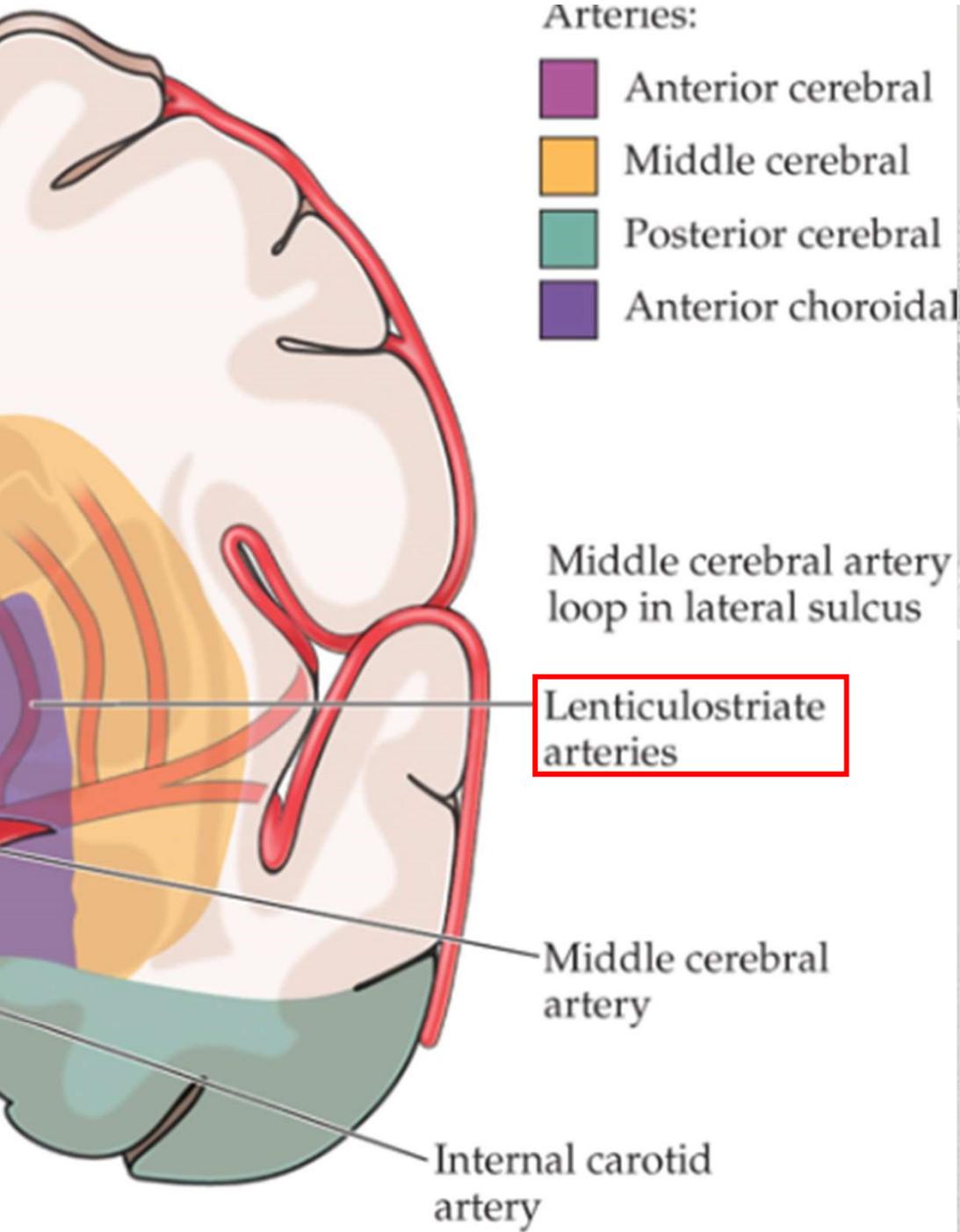
Basal collaterals  $\downarrow$



Total occlusion of ICA & basal collaterals

**Table 2. Suzuki Grading System.\***

Grade	Definition
I	Narrowing of ICA apex
II	Initiation of moyamoya collaterals
III	Progressive ICA stenosis with intensification of moyamoya-associated collaterals
IV	Development of ECA collaterals
V	Intensification of ECA collaterals and reduction of moyamoya-associated vessels
VI	Total occlusion of ICA and disappearance of moyamoya-associated collaterals



# Disease progression: slow but progressive

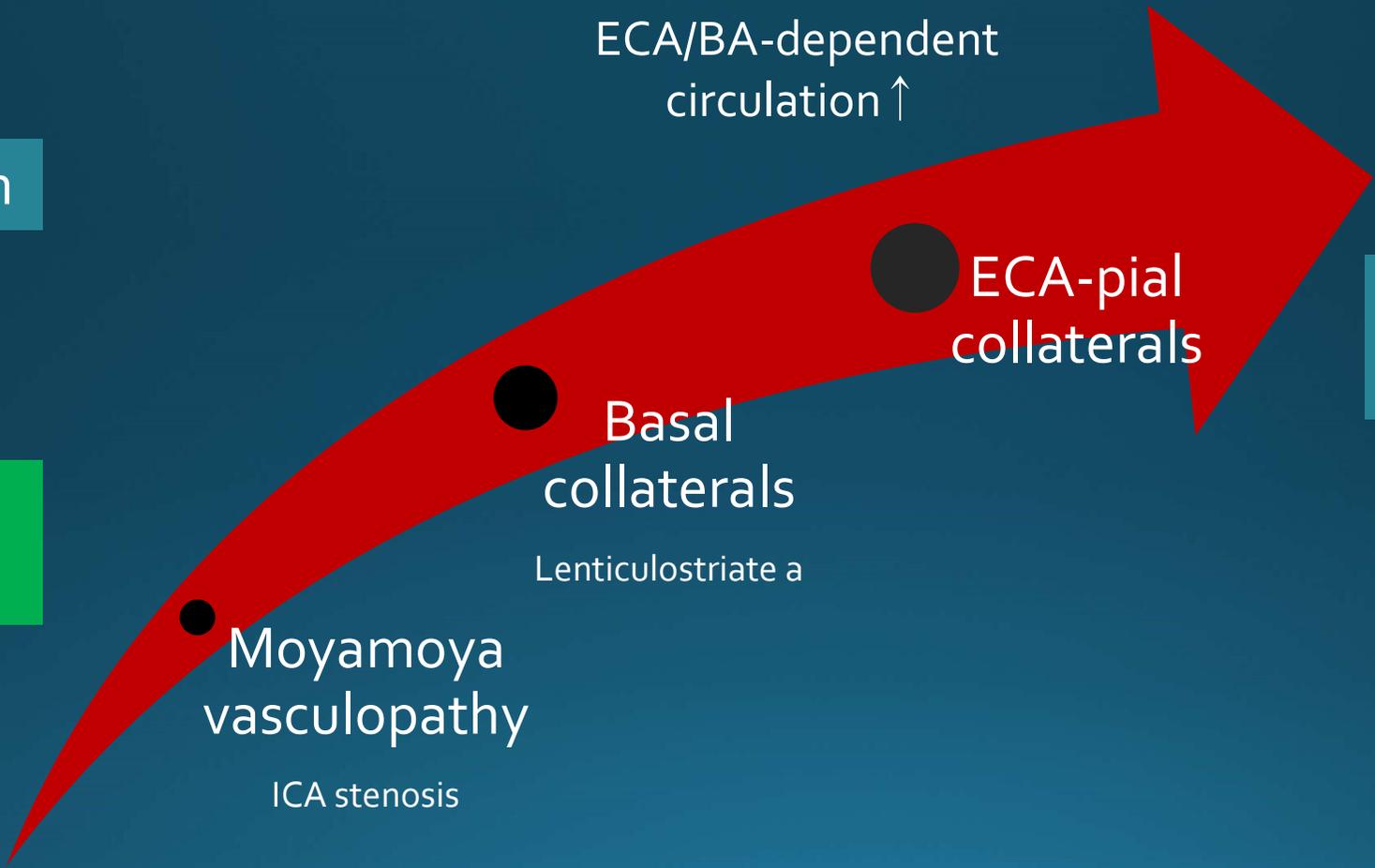
Hyperventilation



Ischemic manifestations

Ischemic stroke  
TIA  
Seizure

ECA/BA-dependent circulation ↑



Moyamoya vasculopathy  
ICA stenosis

Basal collaterals  
Lenticulostriate a

ECA-pial collaterals

Collateral-related manifestations

Hemorrhage  
Headache

ICA: internal carotid artery, BA: basilar artery  
TIA: transient ischemic attack, ECA: external carotid artery

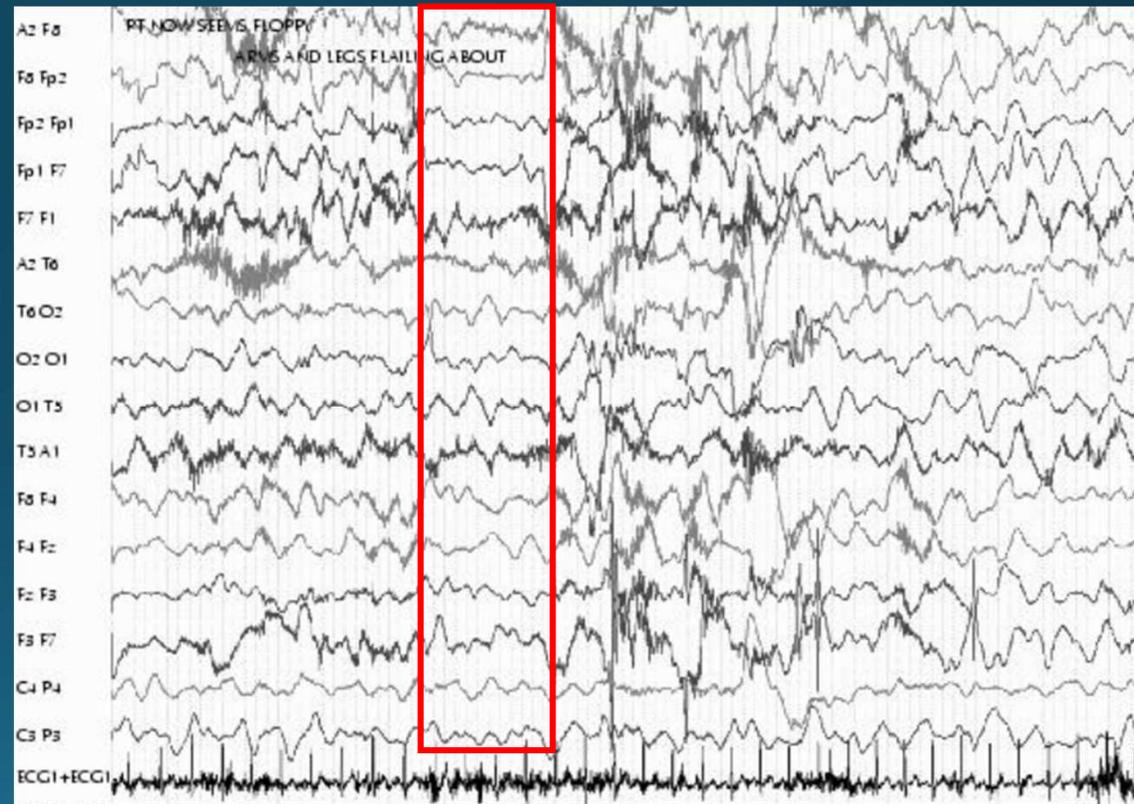
# Clinical manifestations

# Ischemic vs. collateral-related

- *Ischemic* manifestations: provoked by **hyperventilation**
  - Ischemic stroke (50%-75%): low CBF, poor outcome, in kids ↑
  - TIA (50%-75%), seizure (**20%-30%, 2/3 focal**): relatively preserved CBF
- *Collateral-related* manifestations
  - Hemorrhage: 10%-40%, in ventricles & BG, d/t fragile basal collaterals ± aneurysm (BA), in adults ↑
  - Headache: 22%-67%, migraine-like, d/t dilated ECA-pial collaterals
  - Choreiform movements: rare, d/t dilated basal collaterals

# Hyperventilation: a predisposing factor

- Hyperventilation-related situations
  - Hyperventilation:  $\uparrow$  cerebral ischemia
  - Ex: **crying, hot food, fever...**
  - $\text{PaCO}_2 \downarrow \rightarrow$  cerebral vasoconstriction  
 $\rightarrow$  cerebral perfusion  $\downarrow$
- “Re-build up” phenomenon
  - Characteristic monophasic slow waves on EEG after hyperventilation
  - $\downarrow$  Cerebral perfusion reserve



# A typical patient is...

A child aged 5-8 y  
presenting with “stroke” or focal seizure  
provoked by  
hyperventilation-related situations

# Neuroimaging & treatment

# Neuroimaging

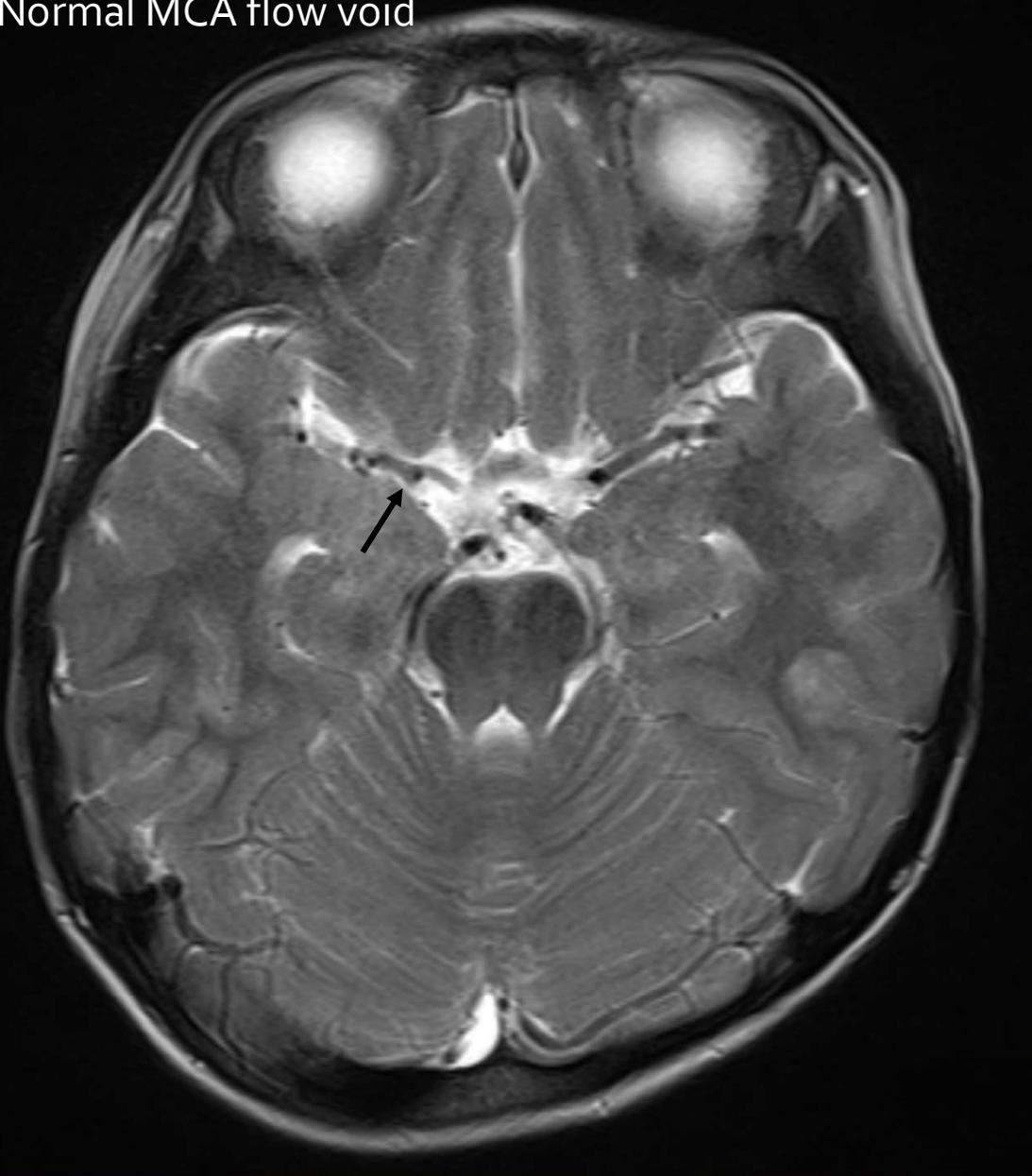
- *Best imaging tools*: focal neurologic deficits/seizure
  - At ED: **MRI plus MRA**
  - At ward: conventional angiography (“puff of smoke”)
- CT: followed by MRI *plus* MRA
  - Useful in rapid triage (albeit inadequate), headache or for adults
  - Occasionally, subacute/chronic infarct or hemorrhage
- $^{99m}\text{Tc}$ -HMPAO SPECT
  - Functional evaluation of cerebral perfusion
  - Acetazolamide challenge: cerebrovascular reserve

# MR findings

	Findings	Clinical implications
ischemic	Loss of ICA/MCA flow voids on T1/T2	ICA/MCA stenosis
	Attenuated COW on time-of-flight MRA	ICA/MCA stenosis
	High SI on DWI, low SI on ADC	Acute/acute-on-chronic infarct
collateralized	Multiple tiny (“dot-like”) flow voids in BG on T1/T2	Basal collaterals
	Net-like cisternal filling defects	Basal collaterals
	Ivy sign (sulcal hyperintensity) on FLAIR	ECA-pial collaterals

ICA: internal carotid artery, MCA: middle cerebral artery, COW: circle of Willis, DWI: diffusion-weighted image, ADC: apparent diffusion coefficient, SI: signal intensity, FLAIR: fluid-attenuated inversion recovery, ECA: external carotid artery

Normal MCA flow void



Loss of MCA flow void



Normal circle of Willis



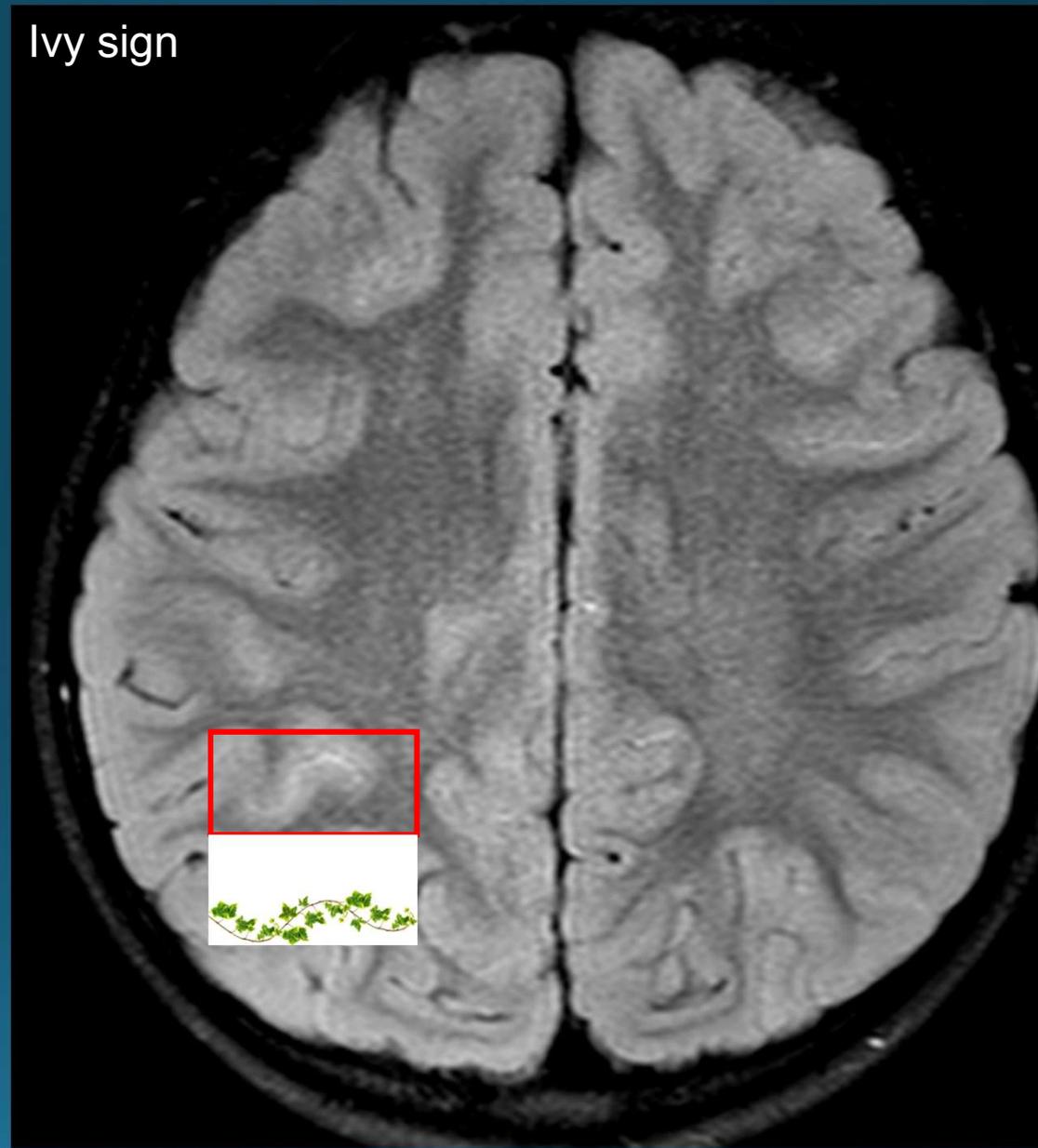
Attenuated circle of Willis



A-pial collaterals



Ivy sign



# Treatment

- Emergent measures
  - Supplemental O<sub>2</sub>, IV hydration (1.5 X maintenance rate)
  - **Avoid** seizure/hypotension/hypovolemia/hyperthermia/hyperventilation
  - Urgent neuroimaging: **MRI *plus* MRA**
  - Aspirin: commonly, but not uniformly used
- Definitive treatment: surgical revascularization (after 6 wk)
  - *Indirect revascularization* (eg, EDAS): commonly used in kids
  - *Direct revascularization* (STA-MCA): severe case or in adults

# Seizure in MIMD

# Seizure in MMD

- Seizure as a presenting manifestation
  - In **20%-30%**, an ischemic manifestation
  - Focal seizure: **2/3** (51/75 from 5 studies)
- More common in toddlers (<1-3 y)
  - Ischemic stroke: ↑ seizure as a presenting manifestation in toddlers (J Pediatr 2011;159:479-83)
  - MMD: seizure is more common in toddlers (Brain Dev 2013;35:569-74)
  - Poor outcome of patients with seizure: <1 y, worse brain lesion/disability (Neurol Med Chir 1993;33:621-4) (J Stroke Cerebrovasc Dis 2015;:17-23)
- Uncommon focal seizure: 5% of 1st seizure & 3% of 1st seizure *plus* fever (Pediatr Neonatol 2010;51:103-111)

# Seizure vs. TIA

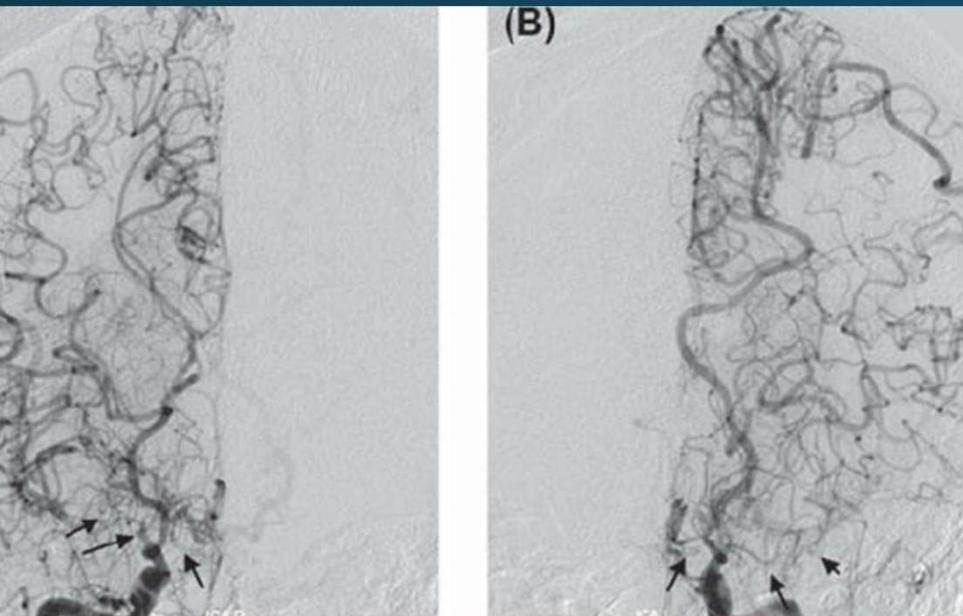
- Something in common
  - Ischemic manifestations implying stroke
  - Seizure/TIA without stroke: relatively preserved CBF & better outcome  
(Childs Nerv Syst 2015;31:713-20)
  - Hard to differentiate seizure from TIA (Neurol Med Chir 1993;33:621-4) (Br J Neurosurg 2012;26:896-8)
- “Limb-shaking” TIA
  - Rhythmic, involuntary hyperkinesia involving unilateral hand-arm-leg
  - Compared to seizure: maybe... ↓ facial involvement & abnormal EEG
  - Indicator of **severe** carotid stenosis (not only in MMD)

SHORT REPORT

## Differential diagnosis between cerebral ischemia, focal seizures and limb shaking TIAs in moyamoya disease

Markus Kraemer<sup>1</sup>, Rolf R. Diehl<sup>1</sup>, Frank Diesner<sup>2</sup>, Peter Berlit<sup>1</sup> & Nadia Khan<sup>3</sup>

9 year-old woman showing intermittent  
parosmia & paresthesia in the left hand



1. Transient marching prickle sensations in the right or left arm → Stop with AED: *Focal seizure*
2. Transient motor aphasia with prickle feelings of the left arm → *TIA*
3. Transient motor aphasia with involuntary shaking of both arms for some minutes → *“Limb-shaking” TIA*

After direct **revascularization**, she remained symptom free for 4 mo. But...

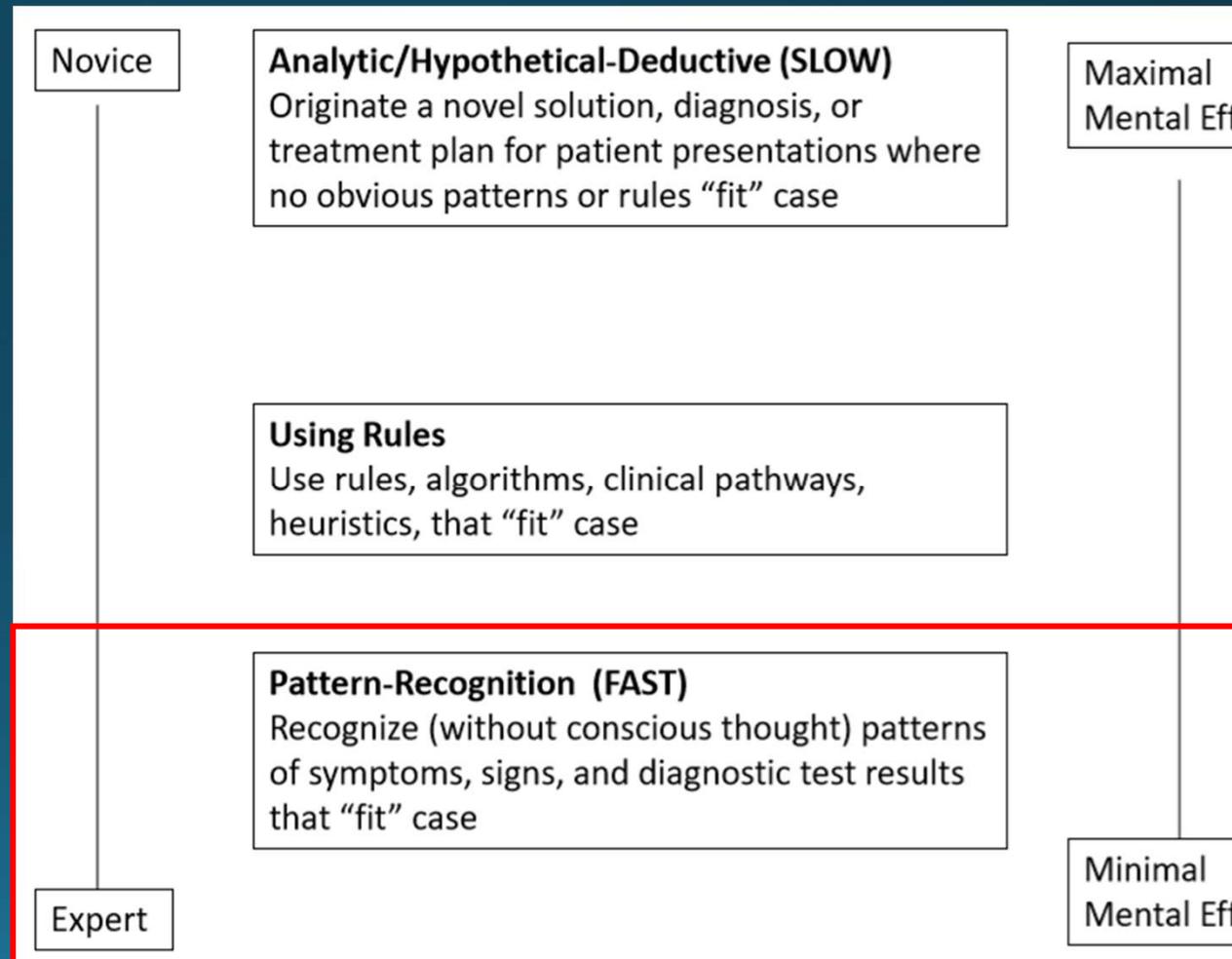
After cessation of AED, **recurrent** attacks of sensory (prickle feelings) marching sensations of the left hand, arm and face at frequencies of 2-4/mo

# Neuroimaging for seizure

- Indications of *urgent neuroimaging* for 1<sup>st</sup> afebrile seizure (Rose's lecture in PEM Vitals 2017)
  - Persistently altered mental status
  - **Focal neurologic deficits**
  - <1 y
  - Suspicious circumstances
- Seizure (**focal** or associated with **focal neurologic deficits**) needs *urgent neuroimaging*

# Possible obstacles in neuroimaging

- Availability bias
- Confirmation bias
- Anchoring bias
- Limited cognitive ability
- Pressure to minimize workups
- Burnouts



# Take-home messages

- In Japan & Korea: most common & treatable cause of stroke
- Manifestations: ischemic & collaterals-related
- Hyperventilation: a predisposing factor of cerebral ischemia
- Key MR findings: loss of MCA flow voids, attenuated COW, & ivy sign
- In 20%-30%: kids present with seizure (2/3: focal)
- 1<sup>st</sup> focal seizure: go directly to MRI *plus* MRA

Any questions?  
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Thank you for your attention