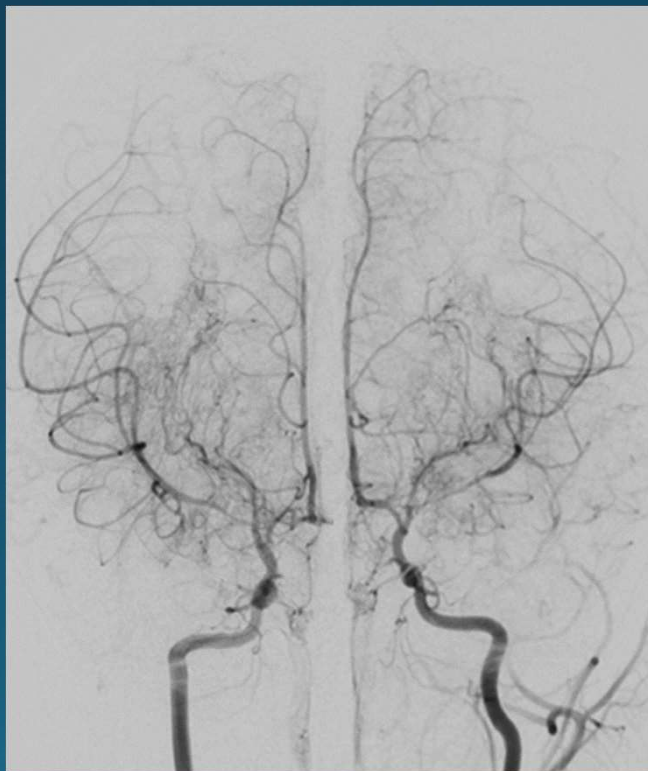
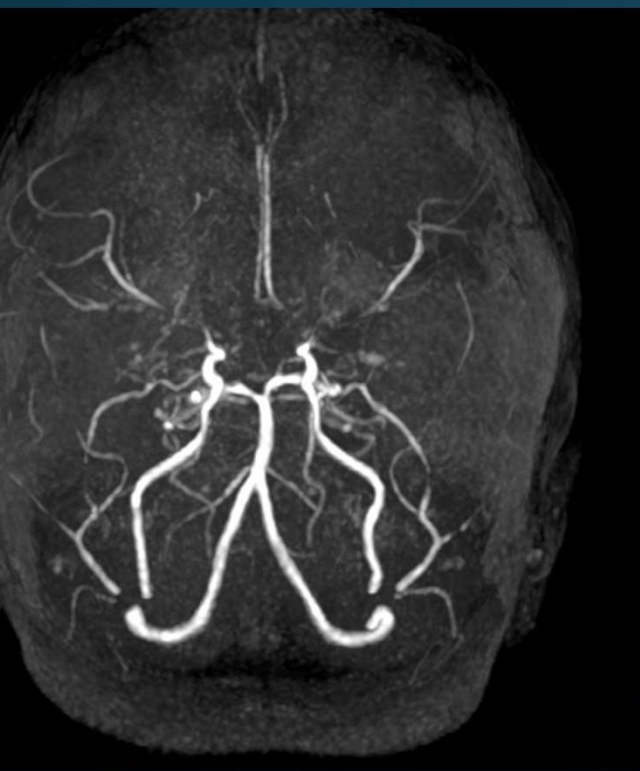


Clinical manifestations of moyamoya disease: seizure in moyamoya disease



서울아산병원
응급의학과
김중현

Things to say about...

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

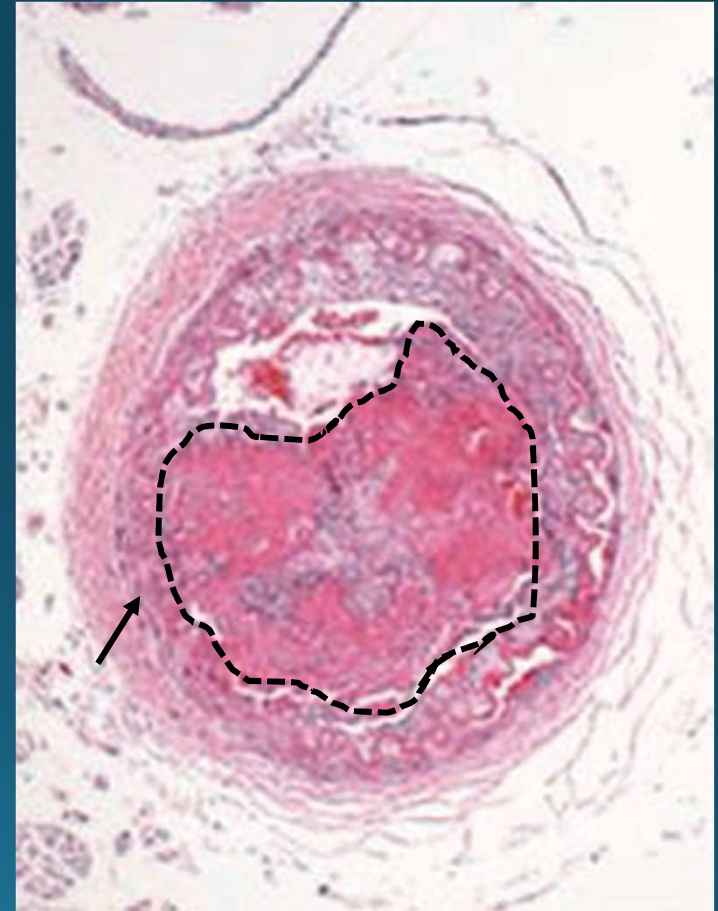
Concepts

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)** & 4th 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



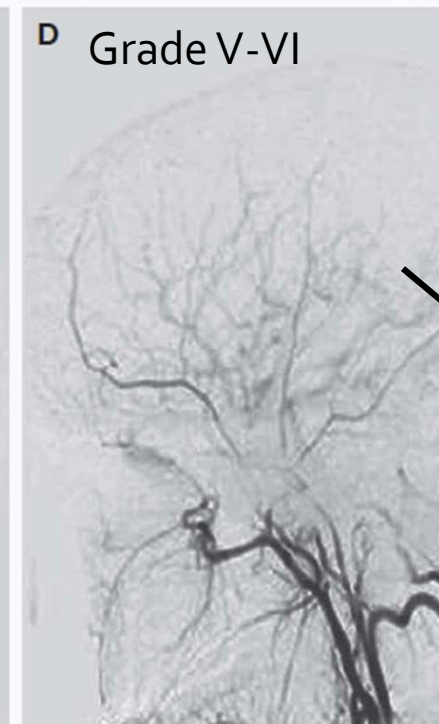
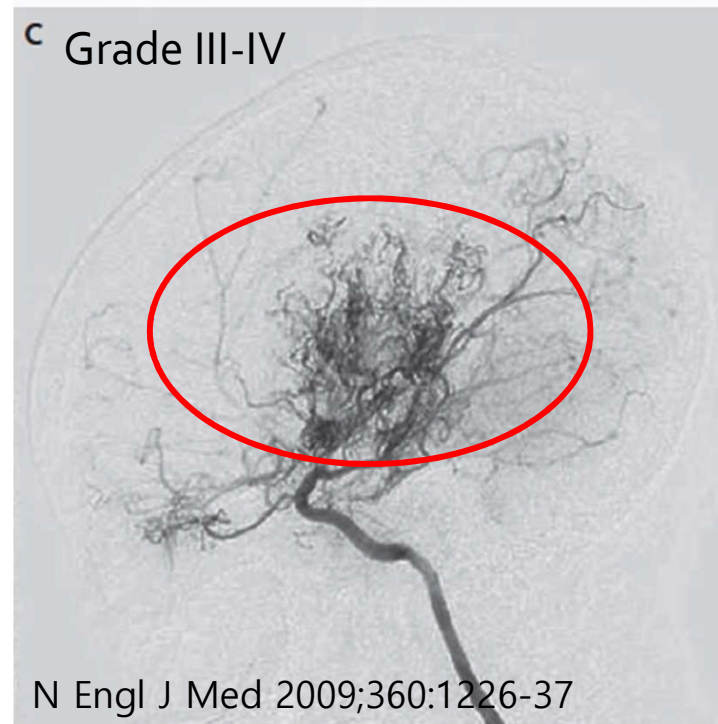
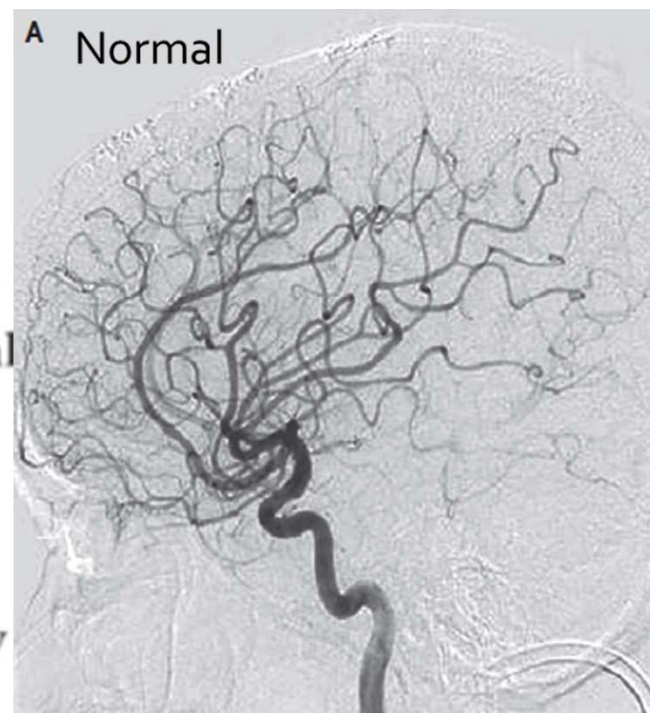
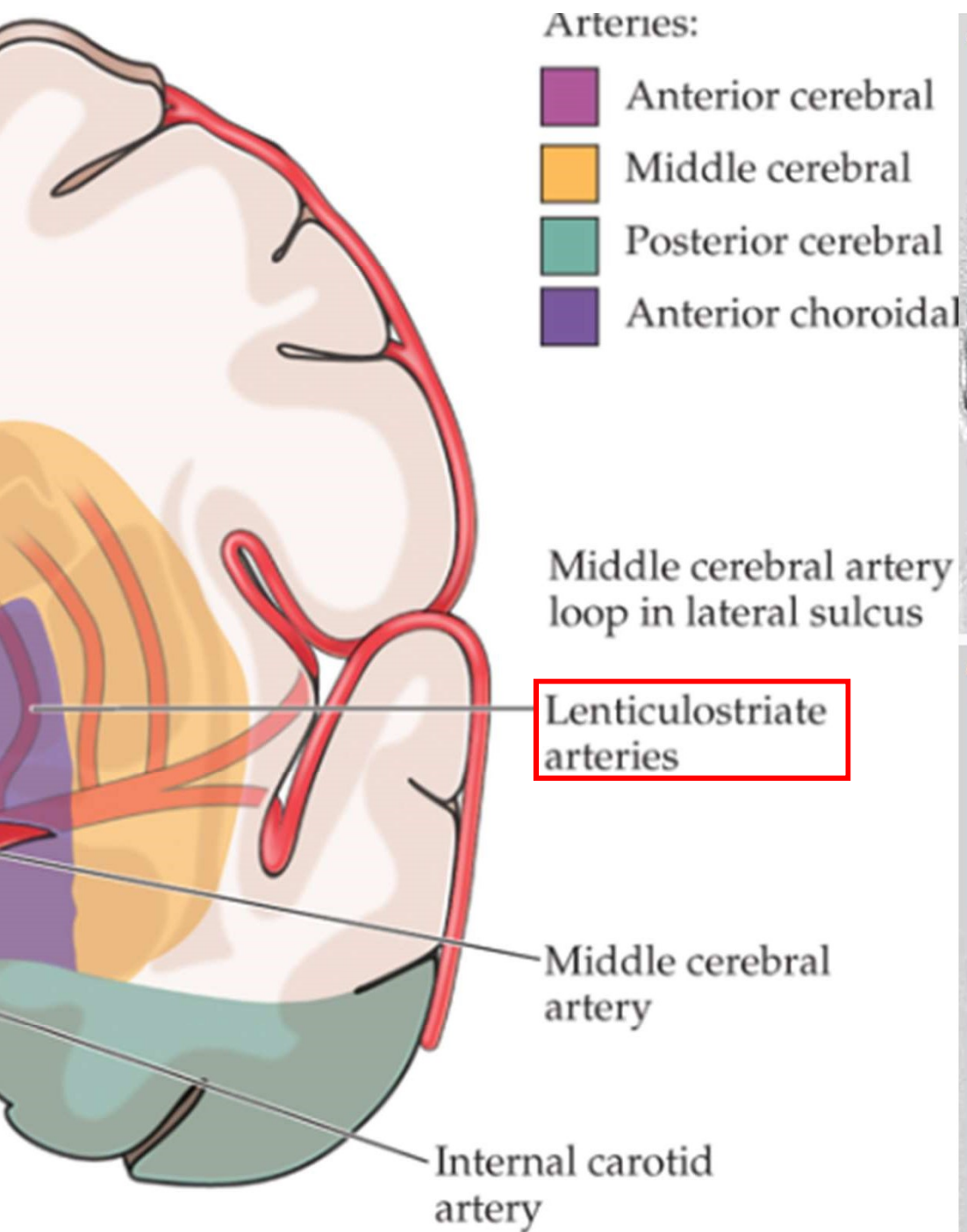
Basal collaterals \downarrow



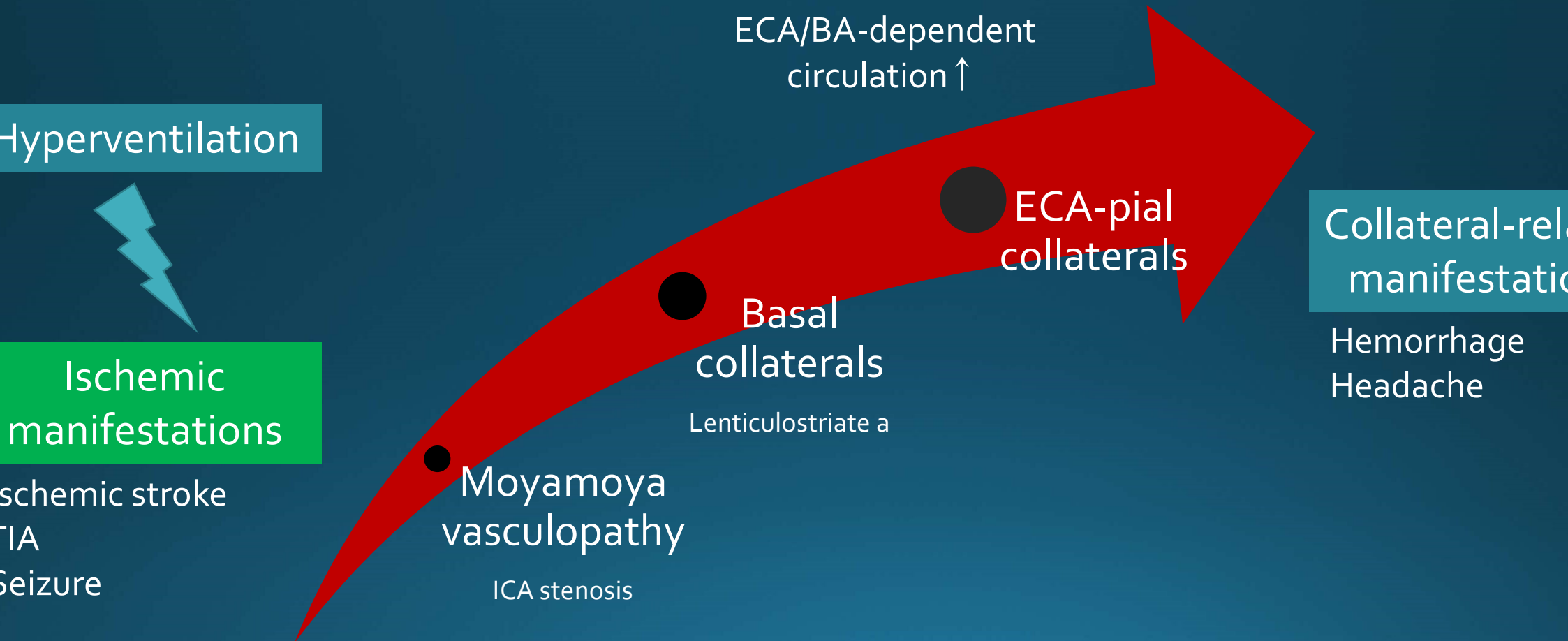
Total occlusion of ICA & basal collaterals

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



Internal carotid artery, BA: basilar artery
Transient ischemic attack, ECA: external carotid artery

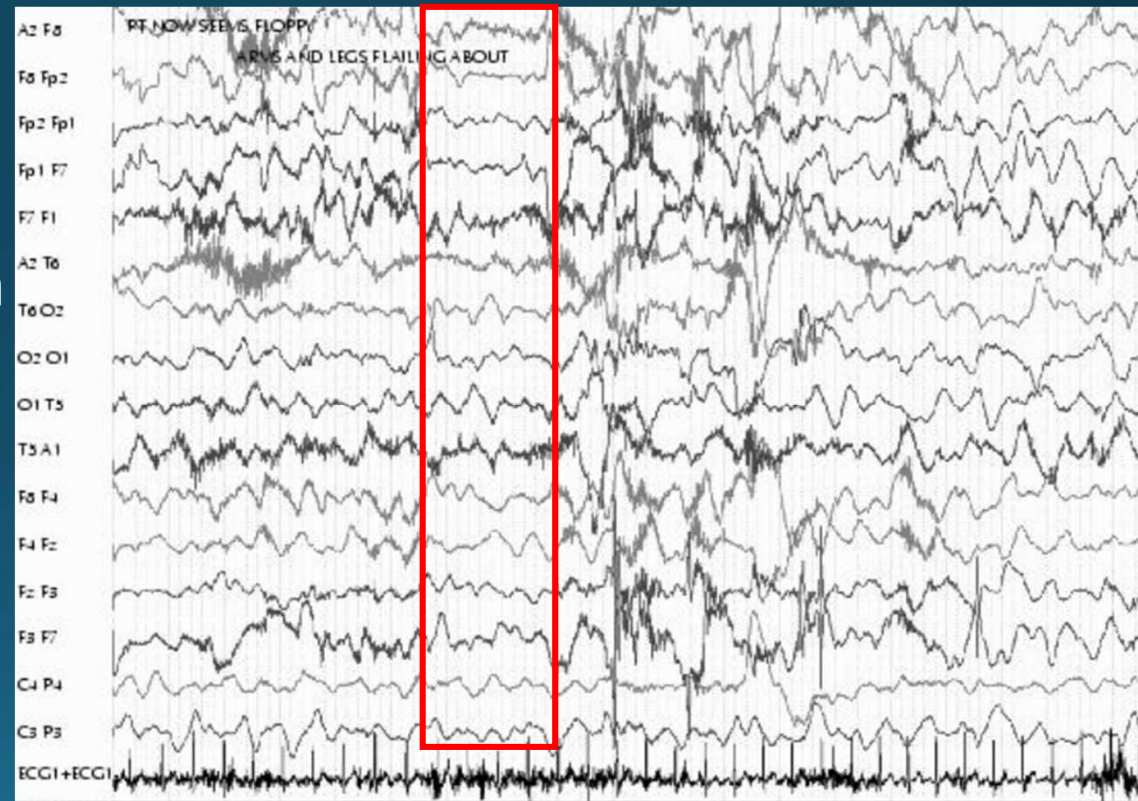
Clinical manifestations

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}Tc -HMPAO SPECT
 - Functional evaluation of cerebral perfusion
 - Acetazolamide challenge: cerebrovascular reserve

MR findings

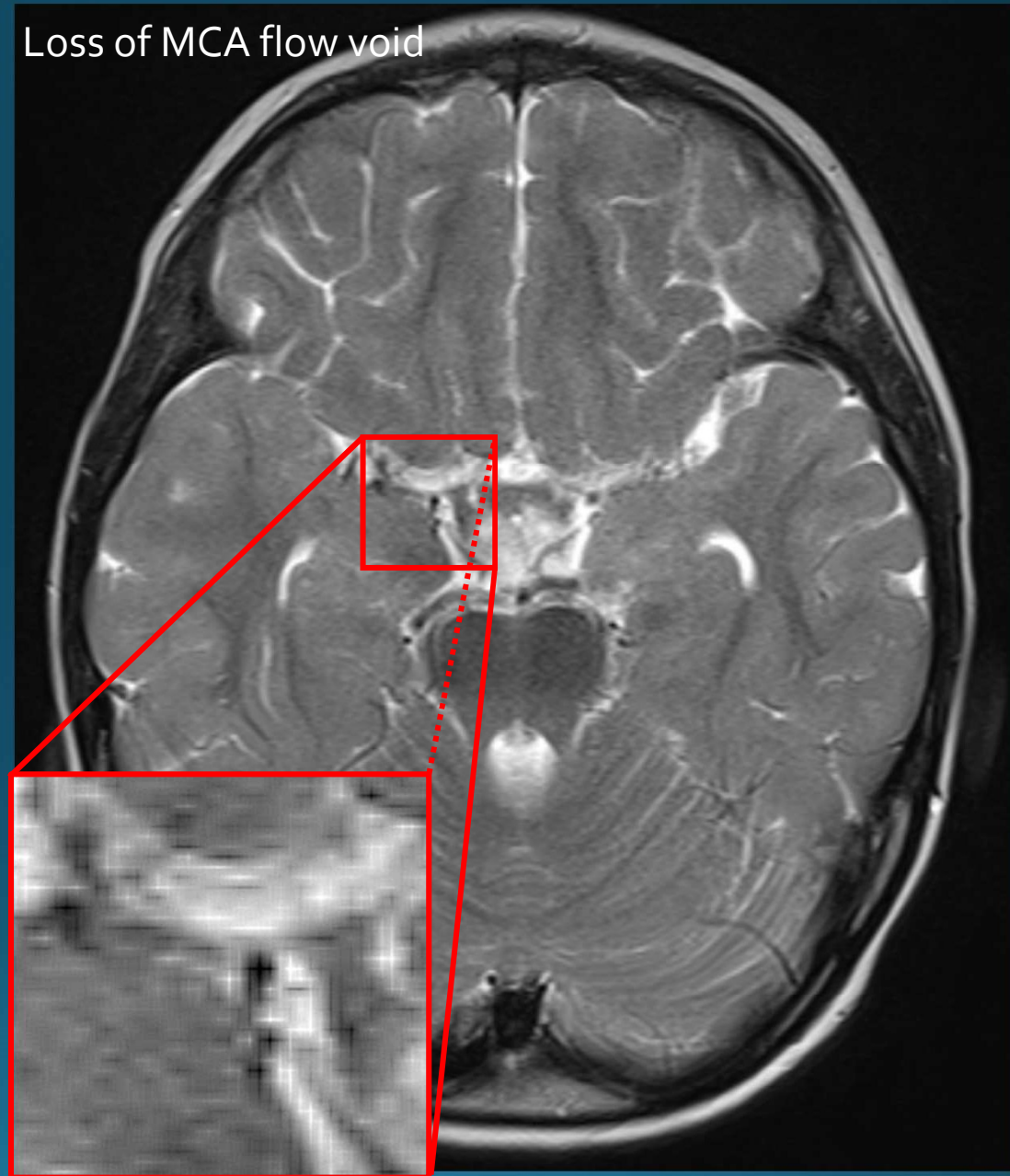
	Findings	Clinical implications
Ischemic	Loss of ICA/MCA flow voids on T1/T2	ICA/MCA stenosis
	Attenuated COW on time-of-flight MRA	ICA/MCA stenosis
	High SI on DWI, low SI on ADC	Acute/acute-on-chronic infarct
Collateralized	Multiple tiny (“dot-like”) flow voids in BG on T1/T2	Basal collaterals
	Net-like 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



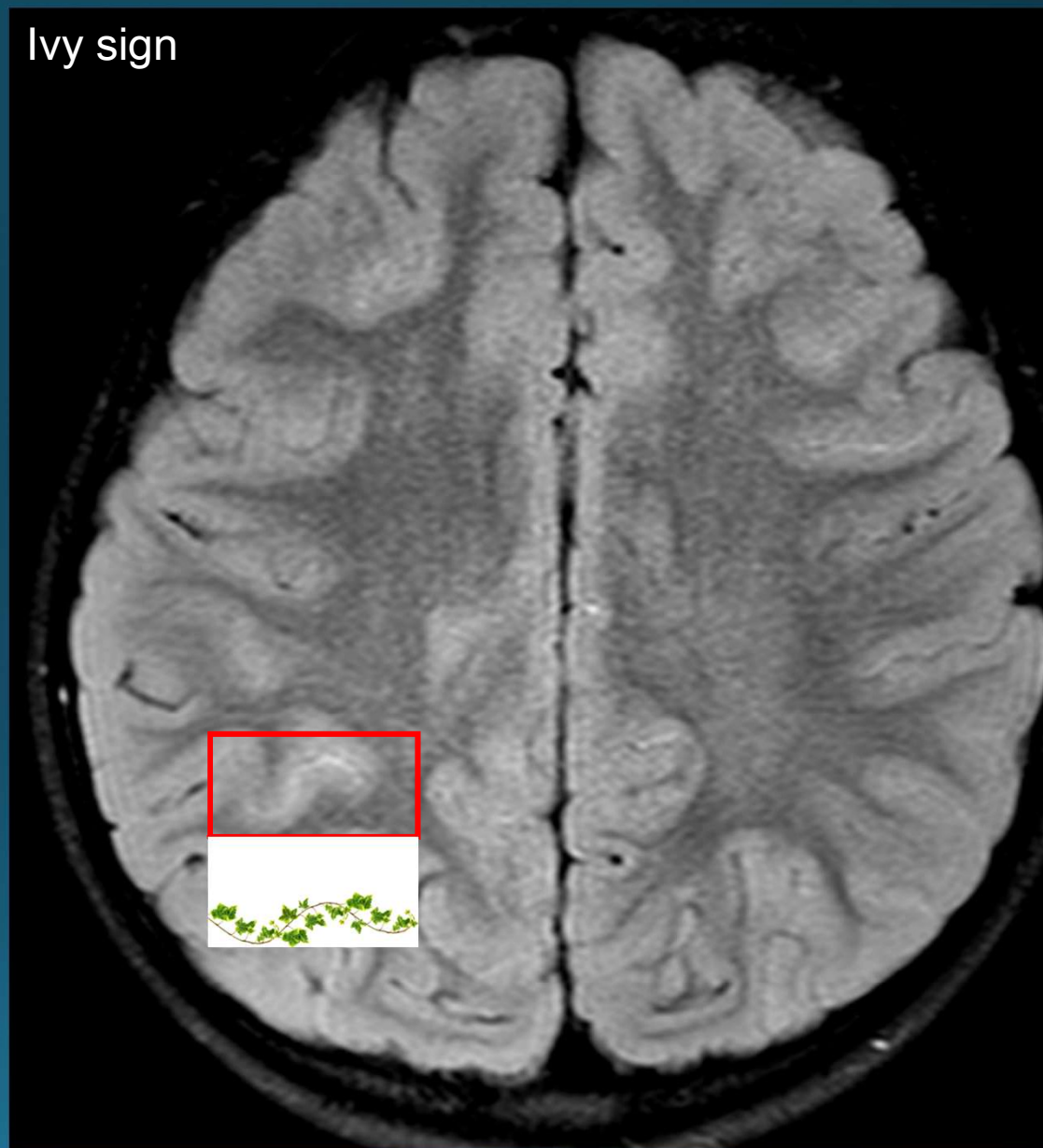
Attenuated circle of Willis



A-pial collaterals



Ivy sign



Treatment

- Emergent measures
 - Supplemental O₂, 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 MMD

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

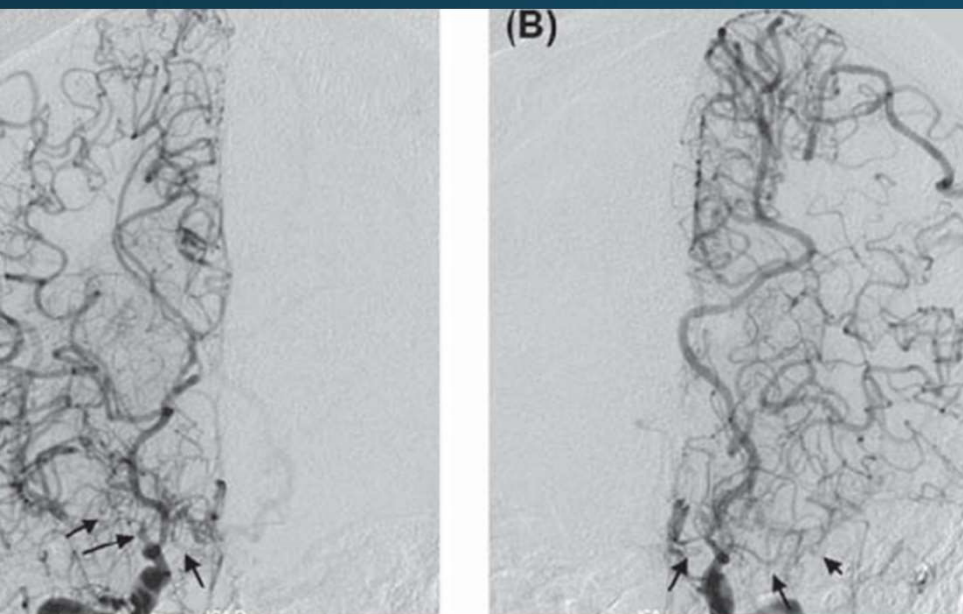
- Something in common
 - Ischemic manifestations implying stroke
 - Seizure/TIA without stroke: relatively preserved CBF & better outcome
(Childs Nerv Syst 2015;31:713-20)
 - Hard to differentiate seizure from TIA (Neurol Med Chir 1993;33:621-4) (Br J Neurosurg 2012;26:896-8)
- “Limb-shaking” TIA
 - 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 Kraemer¹, Rolf R. Diehl¹, Frank Diesner², Peter Berlit¹ & Nadia Khan³

9 year-old woman showing intermittent
motor aphasia & 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...

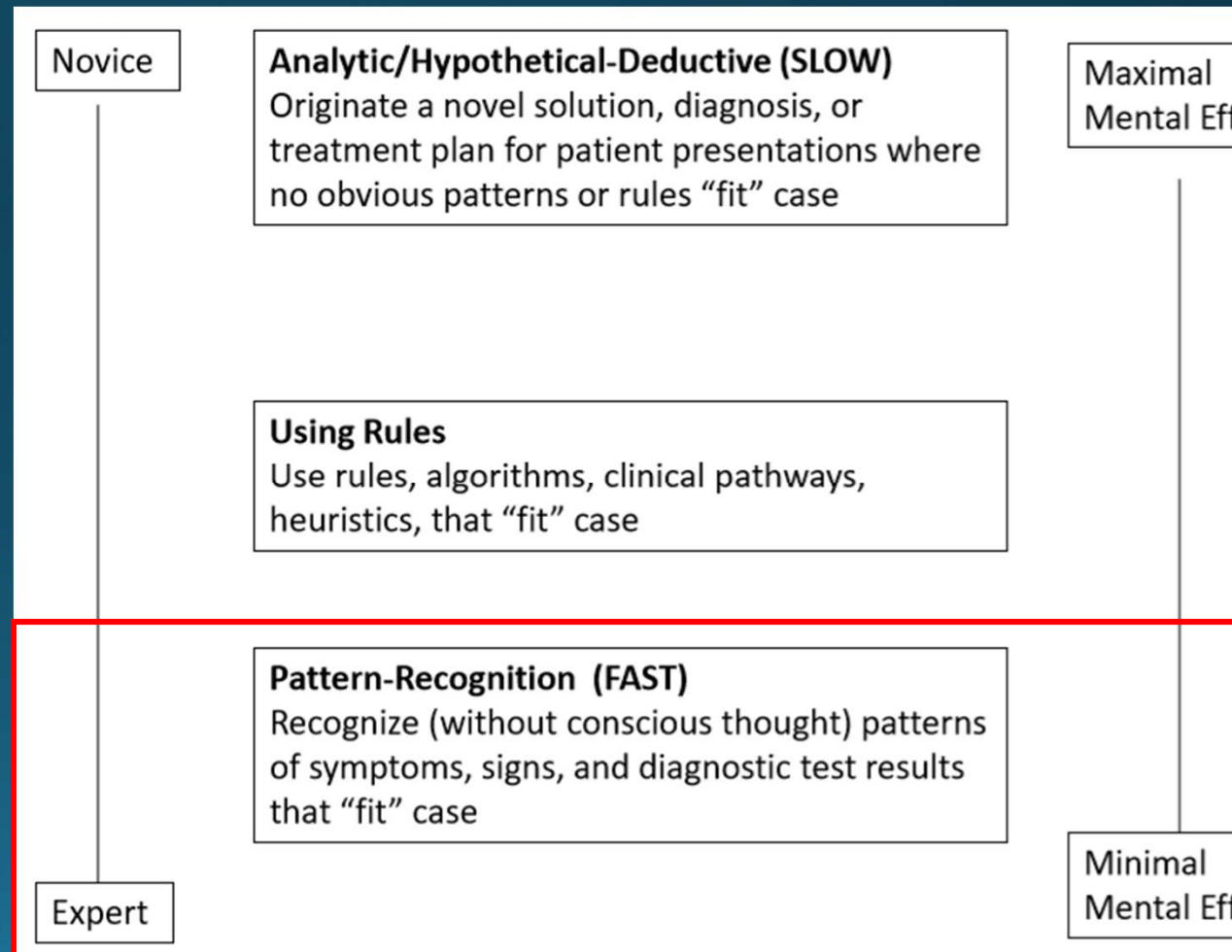
After cessation of AED, **recurrent** attacks of sensory (prickle feelings) marching sensations of the left hand, arm and face at frequencies of 2-4/mo

Neuroimaging for seizure

- Indications of *urgent neuroimaging* for 1st 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)
- 1st focal seizure: go directly to MRI *plus* MRA

Any questions?
medjh@daum.net

Thank you for your attention