

# STROKE, NEUROPLASTICITY and RECOVERY

## A BRIEF OVERVIEW



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# Stroke

*Life's not just being alive, but being well."*

Martial (c AD 40 – c AD 104)

Roman Poet



# Overview

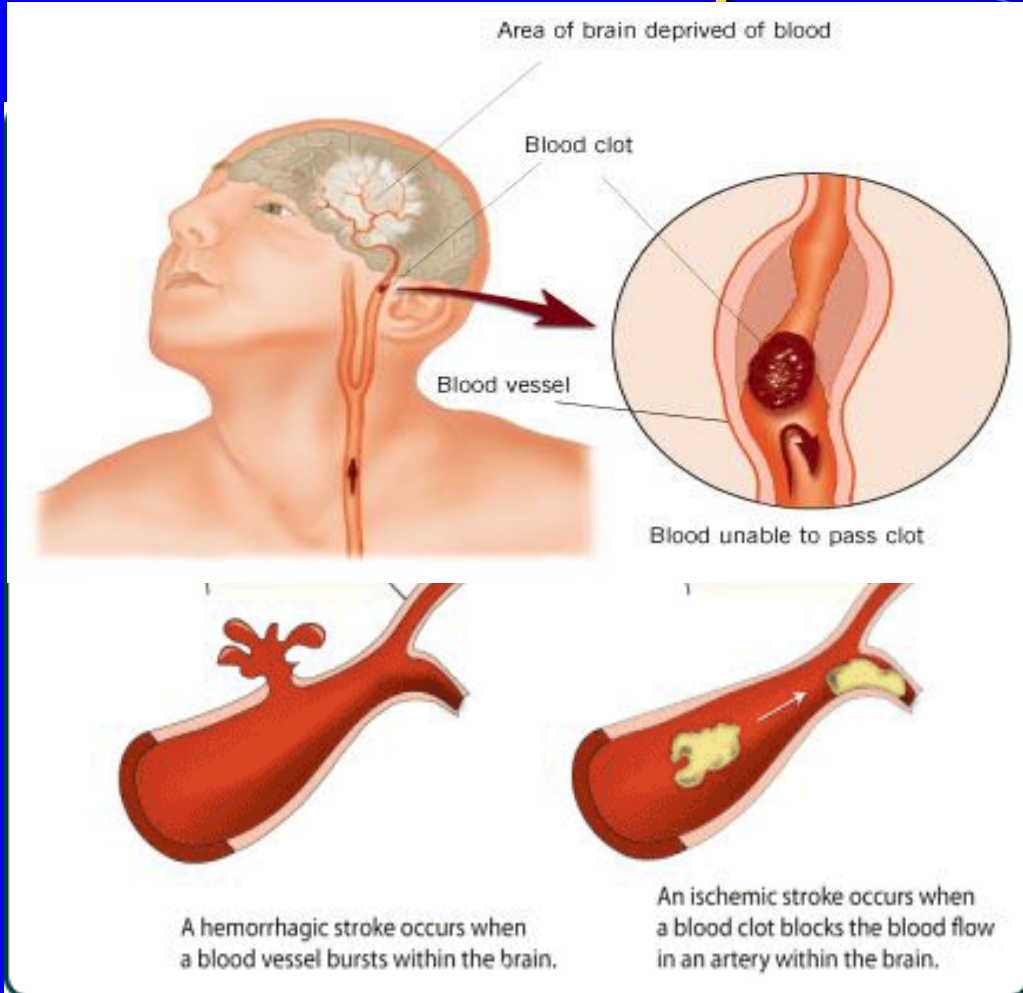
- Stroke is a Hyperacute Medical Emergency
  - FAST and ROSIER
- Time (and affected territory arterial collateral supply) = Brain Cell death = Worse functional outcome
- Increased brain plasticity = Better functional outcomes  
(Neuroplasticity is the ability of the nervous system to adapt in response to intrinsic or extrinsic stimuli by reorganizing its structure, functions, or connections) <sup>1</sup>

# Stroke impact perspective

- Crude incidence of **new strokes: 2.1-2.4/1000 population per year**
  - Rapid increase with increasing age; for every decade after 55, stroke risk doubles 65% of strokes occur over the age of 65yo
    - We can thus predict the number of strokes likely to occur in an area in the following year...
- 4-5% of the National health budget
- 10% of all deaths in the UK (3rd most common cause, highest in hospital cause)
  - Pre-routine Stroke Unit care and thrombolysis, up to 25% of admitted stroke patients died in the first 4 weeks.
    - **Mortality in best units <10% now.**
- **Biggest cause of disability and impairment in the UK**
  - Approx 500,000 stroke / TIA survivors in UK (50% with disability)

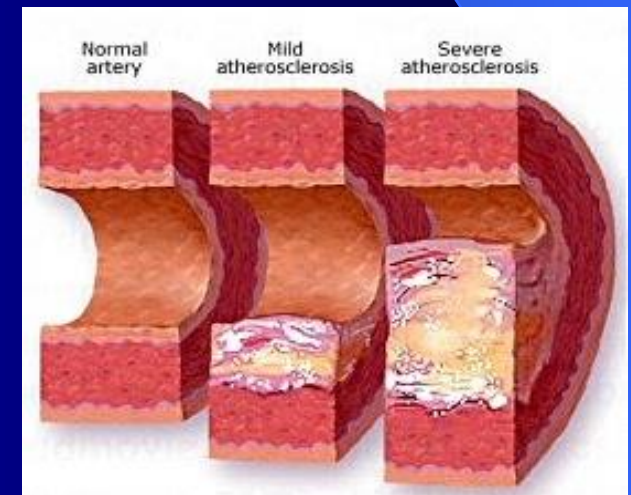
# Stroke pathology

- Cerebral infarction 80%
  - Embolic (atrial fib, valve or carotid disease) 50%
  - Atherosclerotic 30%
- Cerebral haemorrhage 15%
  - Primary intracerebral haemorrhage: 10%
  - Subarachnoid haemorrhage 5%
- Uncertain <5%
- First ever stroke event (2/3<sup>rd</sup> of cases) or Recurrent event (1/3<sup>rd</sup>)



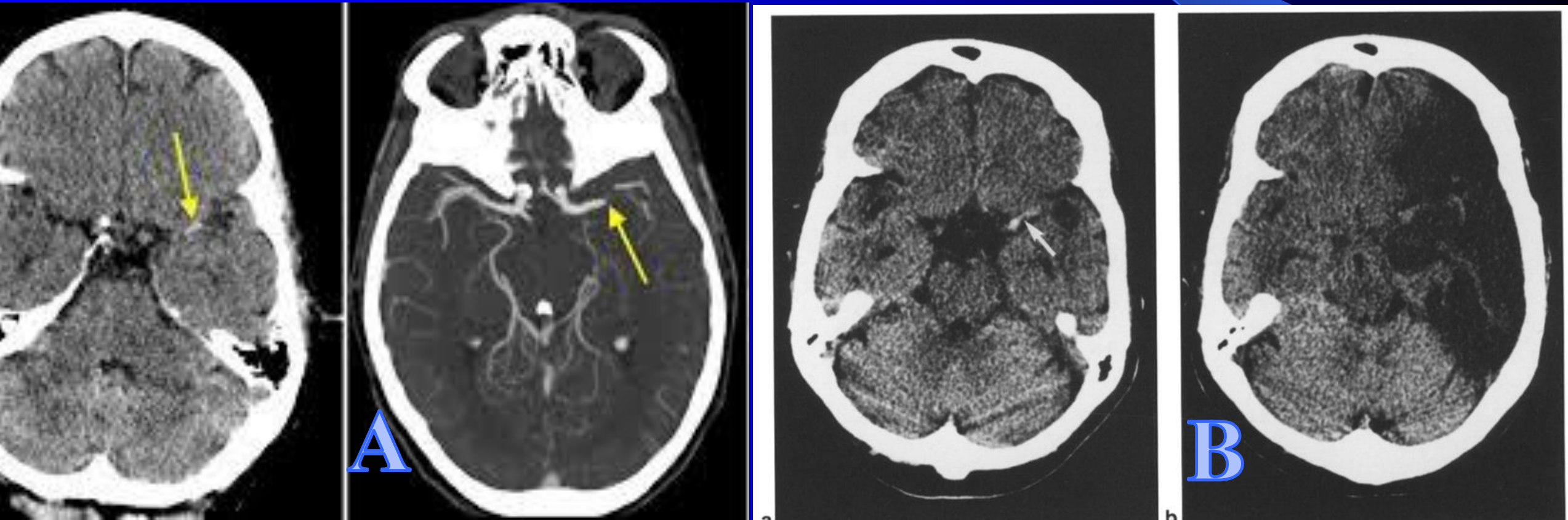
Aneurysm, AVM, amyloid angiopathy etc

Embolism or blockage of narrowed artery



# CT Head and Angiogram

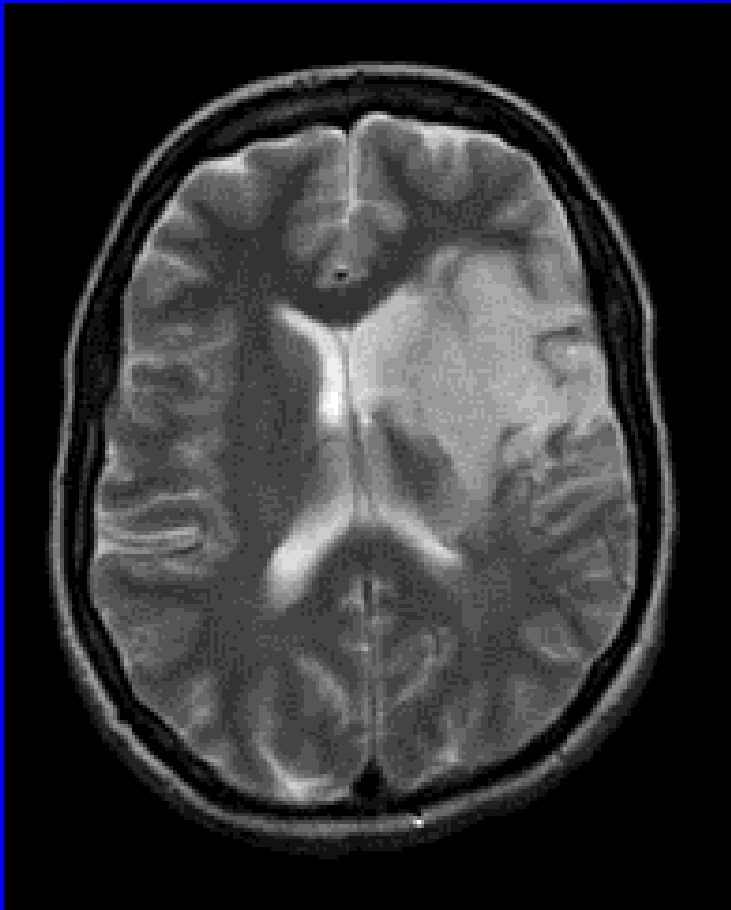
- “Dense” left MCA (middle cerebral artery) signs
- A: CTA MCA cut off sign confirming occlusion
- B : Impact if left untreated



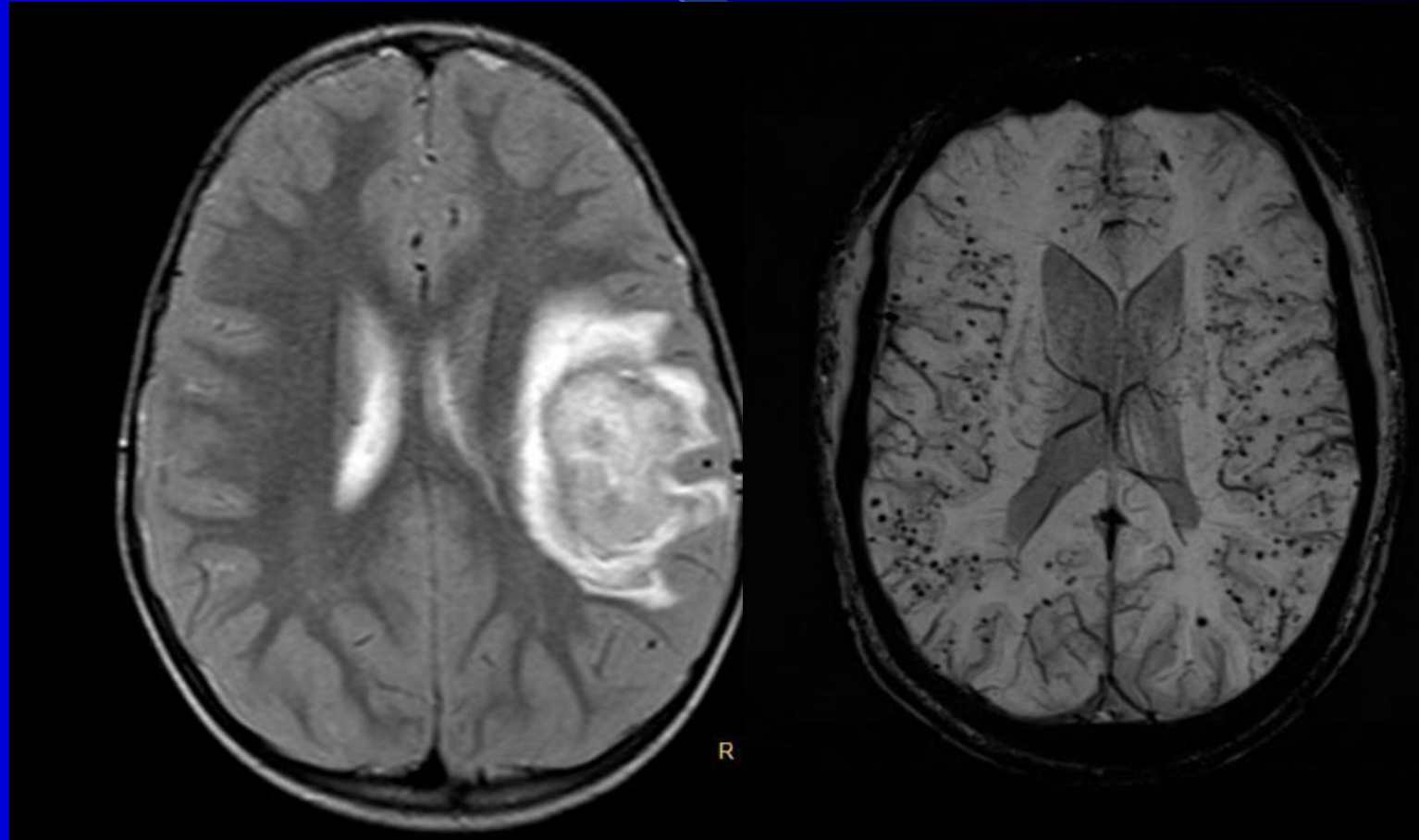
# Standard Imaging Modalities

## Infarct vs ICH

MRI – infarct – Left MCA



MRI – Bleed and Microhaemorrhages

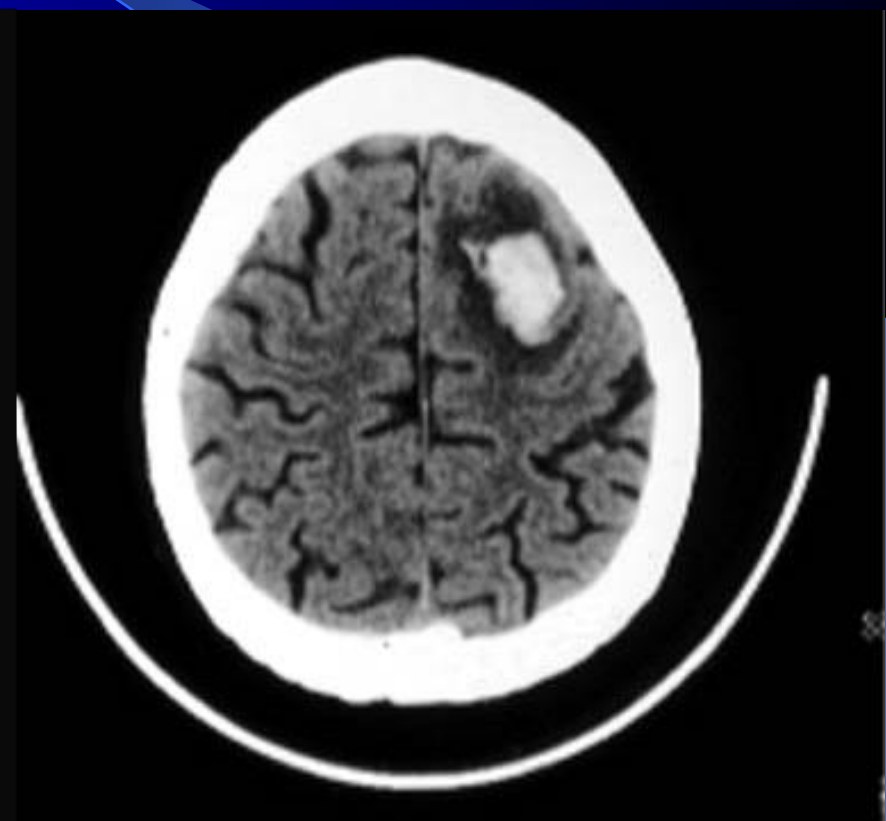
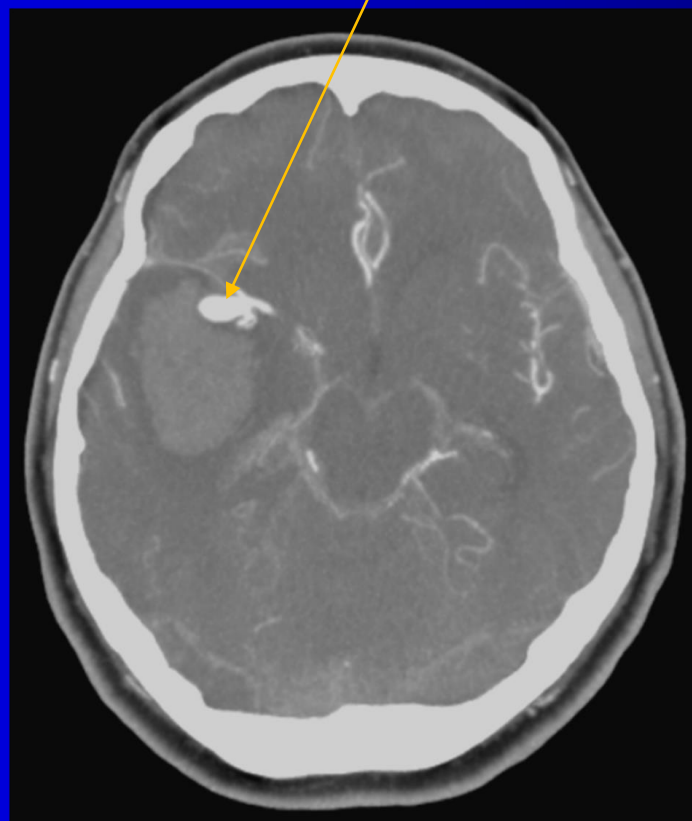


# Infarct vs ICH on CT

Arterial branch territory, wedge shaped, to periphery (note BG calcification –not haemorrhage)

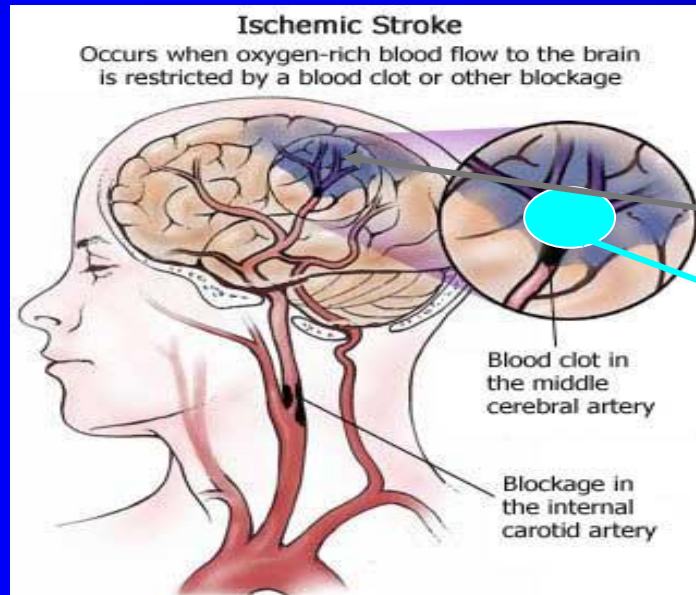
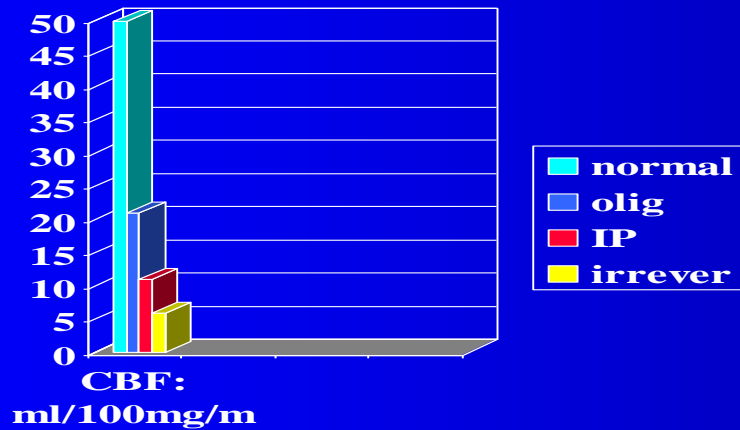
Aneurysm and bleed on CTA ,

Surrounding oedema - black



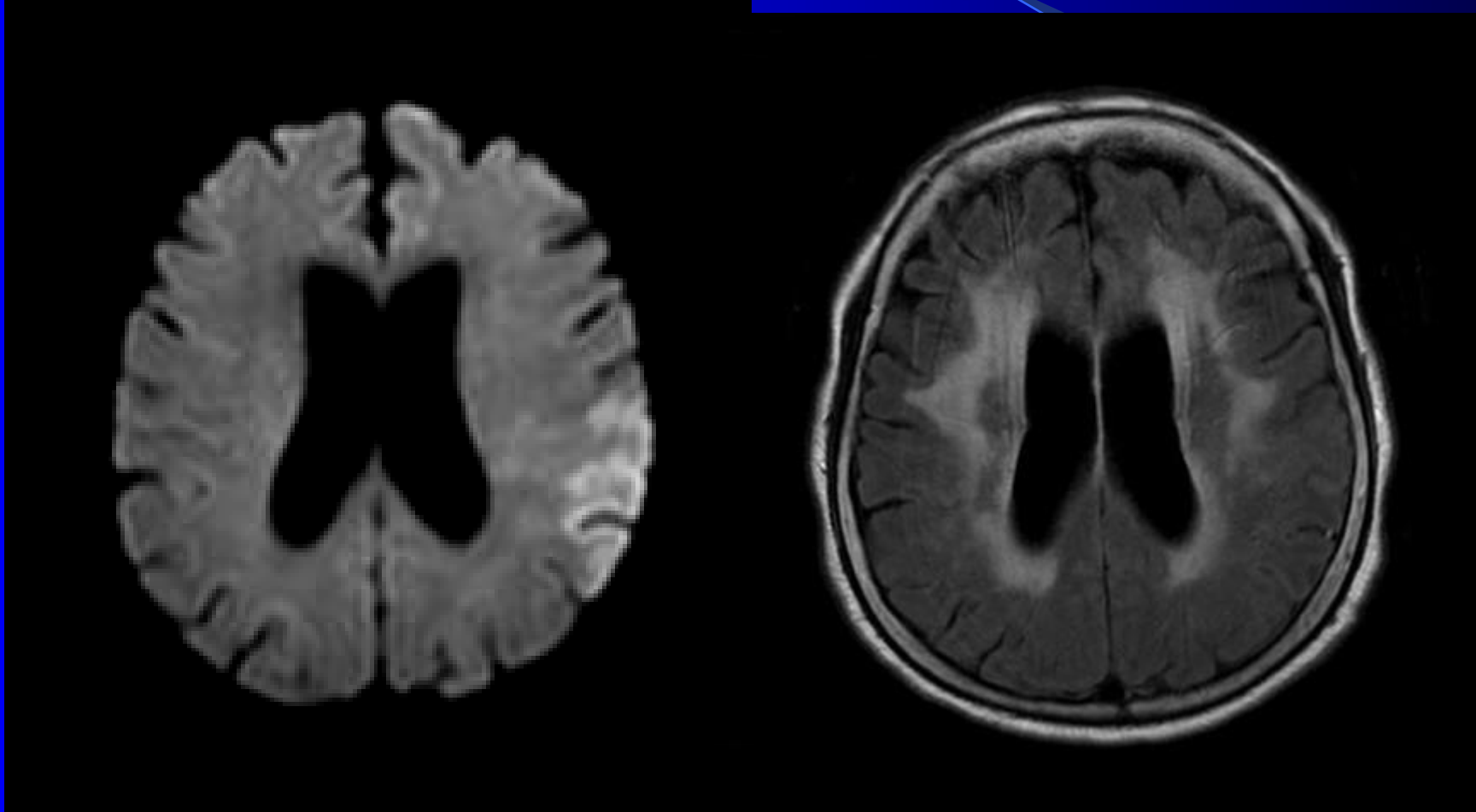


# Cerebral perfusion and penumbra – Time and collateral supply is “Brain”

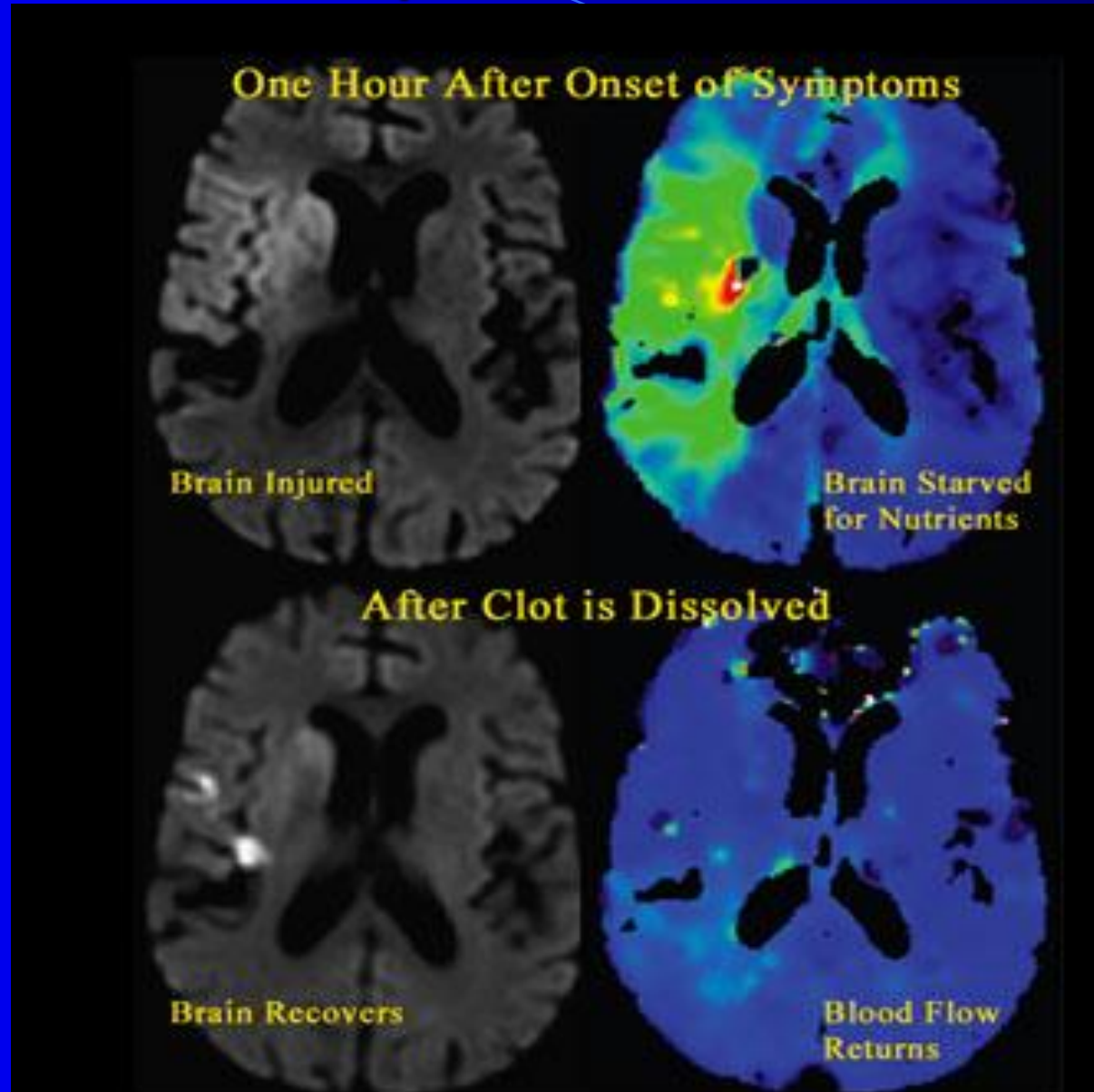


- Normal >50.
- Oligaemia >21: normal neuronal activity.
- Flow dependent on numerous factors:
  - Vessel patency/size
  - BP & cerebral perfusion pressure\* (Anaemia/oxygenation) (\*Degree of cerebral oedema)
- Ischaemic penumbra: functionally silent brain but viable.
  - Time dependent
- Irreversibly damaged tissue.

The diffusion restriction (left) is not already visible in the FLAIR image (right), making the patient “FLAIR negative”



# Functional Scanning – potential early predictor



# Bamford Classification

- Total Anterior Circulation Syndrome – TACS.
- Partial Anterior Circulation – PACS.
- Posterior Circulation – POCS.
- Lacunar Syndrome – LACS.

## NIH Stroke Scale (thrombolysis)

- 15 point scale (max score 42 theoretically)
  - 3 to 5 severity categories per point; scored from 0 (normal)
- Total:  $\geq 4$  and less than 25 **and** no c/i **and** within time (approx 4.5 hrs of *definite* onset) then consider thrombolysis\*

\* Not absolute; exceptions...

# Initial treatment

- Assess for urgent intervention
  - Up to 5 hours post stroke onset, longer in posterior circulation (ischaemic strokes)
  - ASPECTS score >6
- NIHSS / significant functional impact of stroke (dominant hand function loss or dysphasia etc)
- IV Thrombolysis: selected patients (<3hrs, up to 4.5hrs selected cases) : 10-20% of all strokes
  - IA thrombectomy / thrombolysis (selected cases)
  - Expanding intervention – “wake up”/ new imaging modalities
- Urgent reversal if on anticoagulants and bleed suspected and INR elevated/DOAC levels elevated.

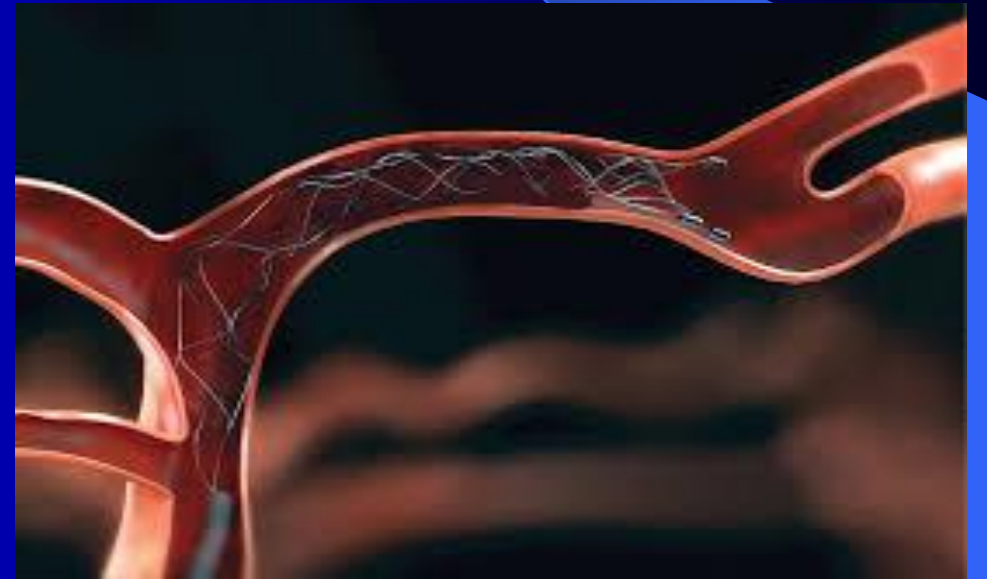
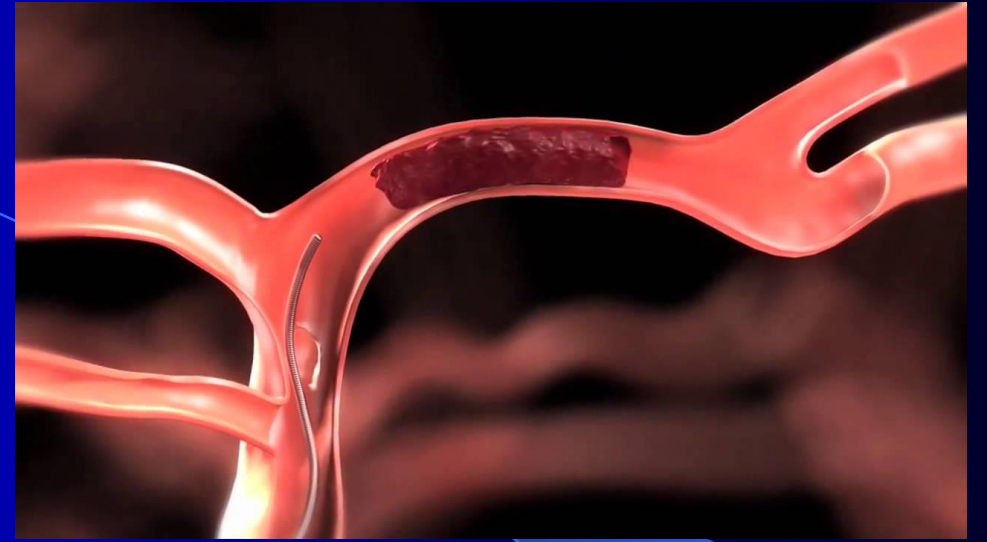
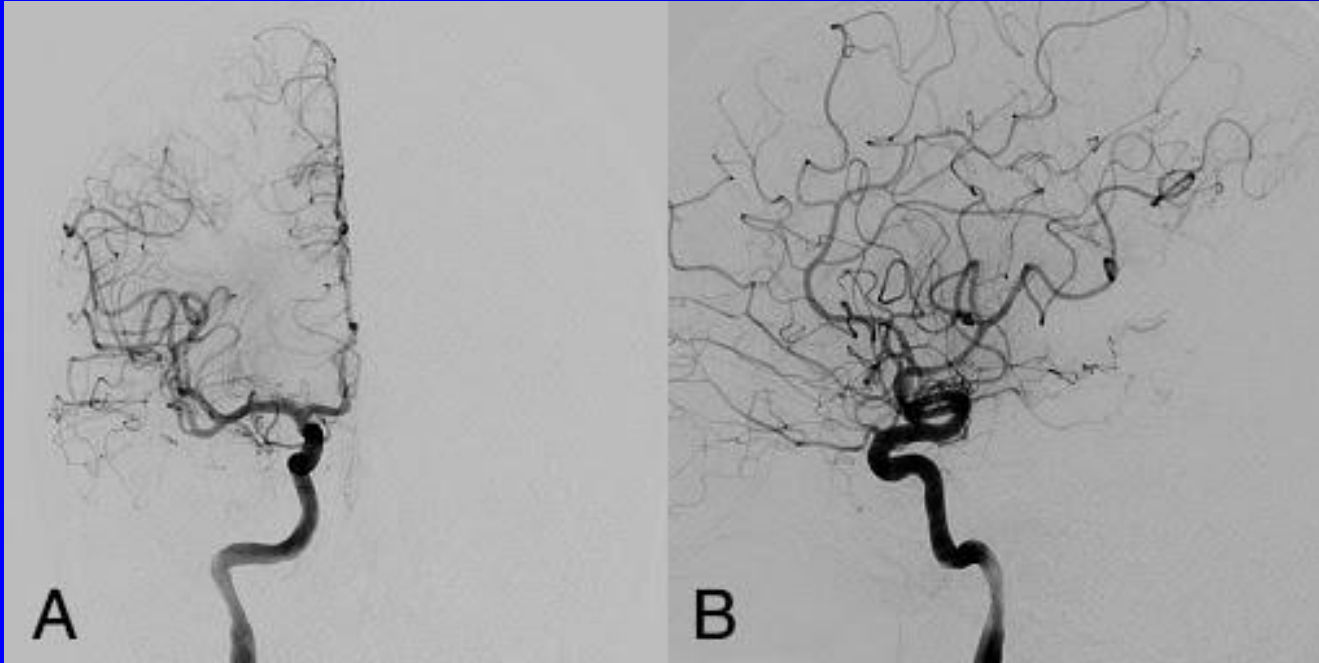
# Aneurysm Acute Intervention



**Coiling of large basilar aneurysm**



# Mechanical Thrombectomy



A: angiogram showing poor arterial filling.  
B: angiogram showing arterial filling after thrombectomy.

# OUTCOMES - overview

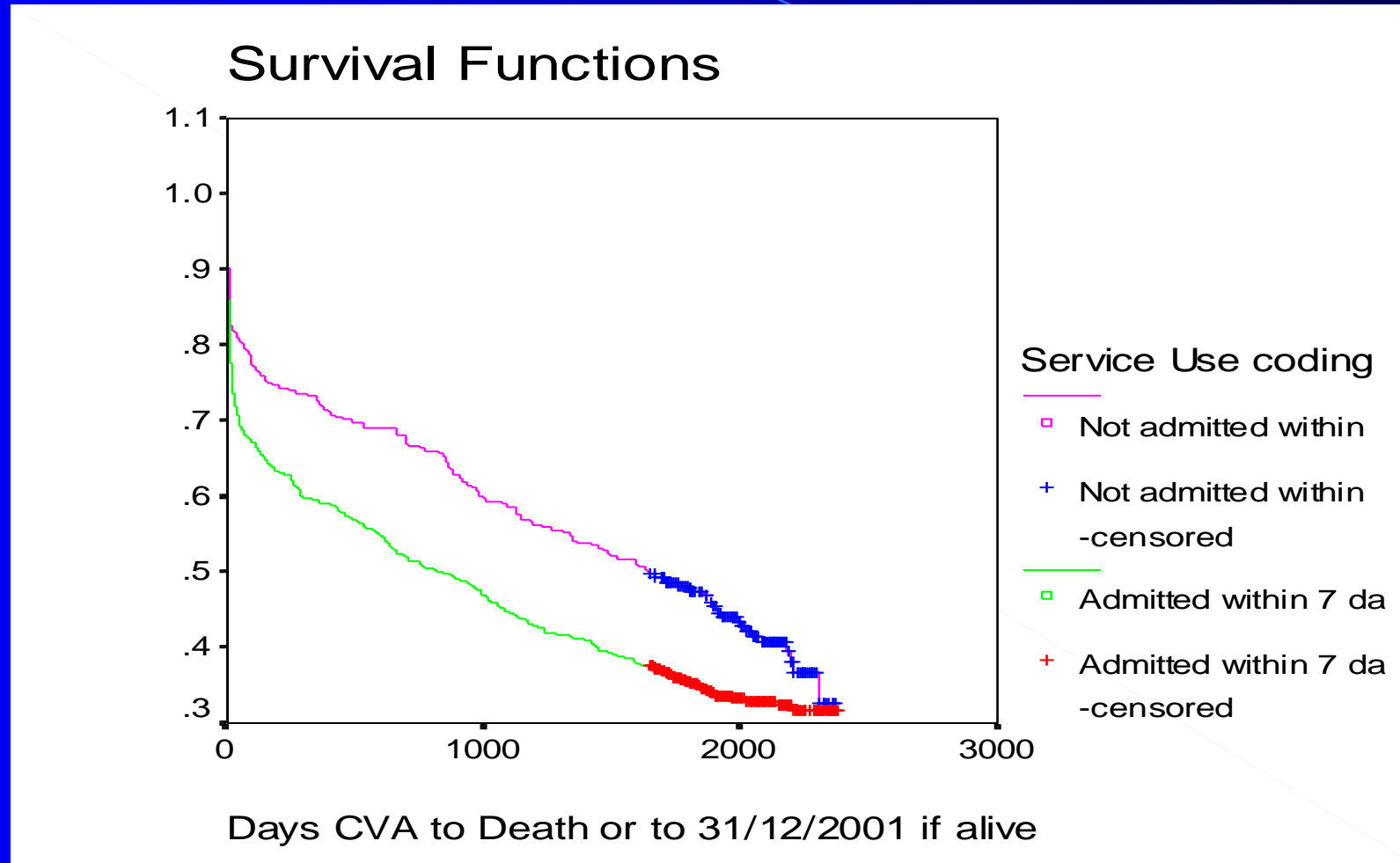
Mortality

Predictors of recovery

Independence levels / Place of residence



# Long Term survival: 4 years.



Mortality (% , n=1010, FES, ICH and CI, excl SAH).

Post stroke	TACS	PACS	POCS	LACS
24 hours	7	0	3	0
28 days	57	8	25	0.5
6 months	69	16	33	6
12 months	74	20	36	8

# Predictors of poor recovery.

- Older age.
  - Incontinence.
  - Visuospatial deficits.
  - Symptomatic co - morbidities.
  - Greater severity.
- 
- Poor survival.
  - Severity of stroke.
  - Co - morbid disease.
  - Older age.
- 
- Institutionalization.
  - Absence of a partner.
  - Severity of disability.
  - Older age.

# Functional (%) outcome – OCSP (FES, CI only): remainder deceased.

Time	LACI	TACI	PACI	POCI
<u>30 days</u>				
Depend	36	56	39	31
Indep	62	4	56	62
<u>6 m</u>				
Depend	26	39	34	18
Indep	66	4	55	68
<u>12 m</u>				
Depend	28	36	29	19
Indep	60	4	55	62

# Why do patients get better?

- Rehabilitation:
- refers to the lessening of *activity limitations and participation restrictions* associated with neurological injury.
- Prolonged time scale.
- Multifactorial
- **Goal setting - individualised**

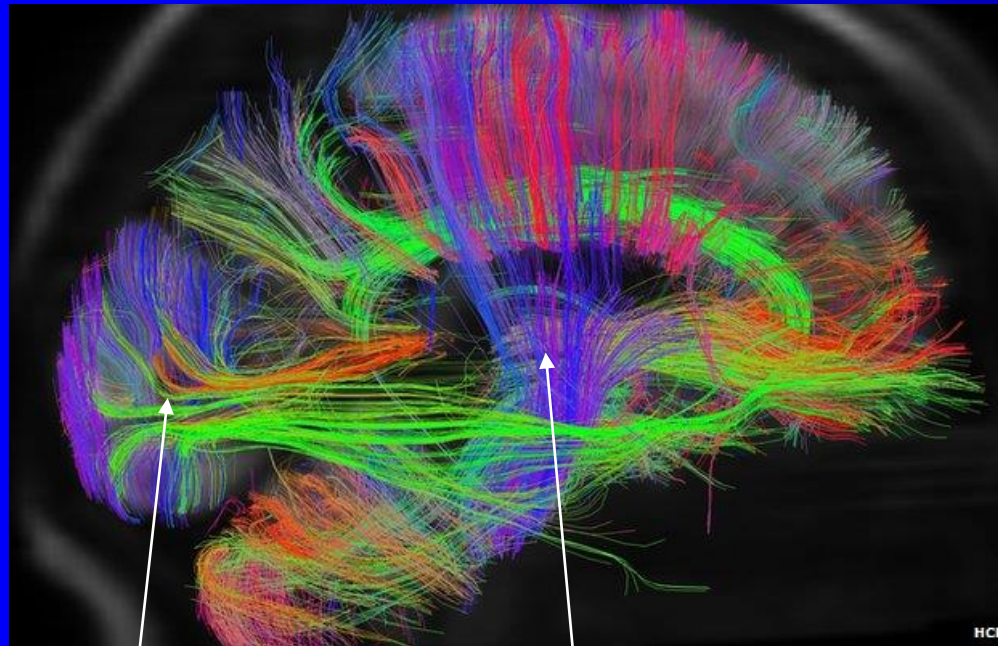
# Neurological recovery

- Patient's initial neurological deficit and premorbid deficits are critical factors.
  - Aetiology of stroke etc.
- Potential theoretical mechanisms
  - 3 Rs. - Restorative neurology.
    - Replace cells.
    - Regrow axons, dendrites and synaptic connections.
    - Retrain circuits, networks and behaviour.
- Stem cells?

# Ever changing intricate brain connections

changes occur after each experience:  
an ever changing record of who we are and what we have encountered\*

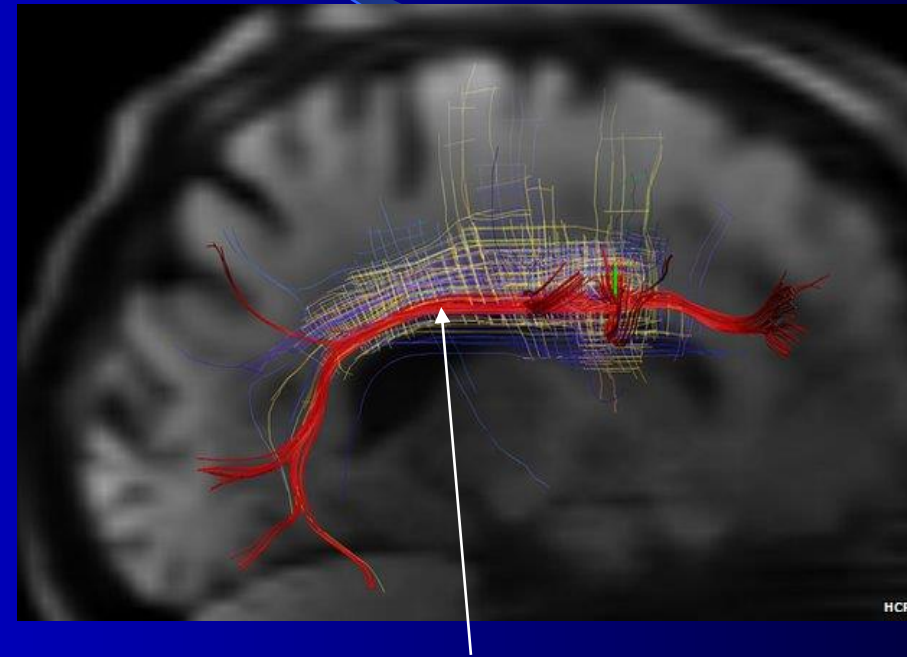
Right side view of brain pathways



Visual Cortex:  
connected by large  
bundle (green) to  
frontal lobes.

Centre, vertical pathways (blue)  
voluntary movement –  
connecting motor cortical areas  
via internal capsule to spinal  
cord.

View of the left hemisphere, the major pathway of language



Organised as part of a regular grid of  
pathways. “Arcuate bundle” is coloured red.

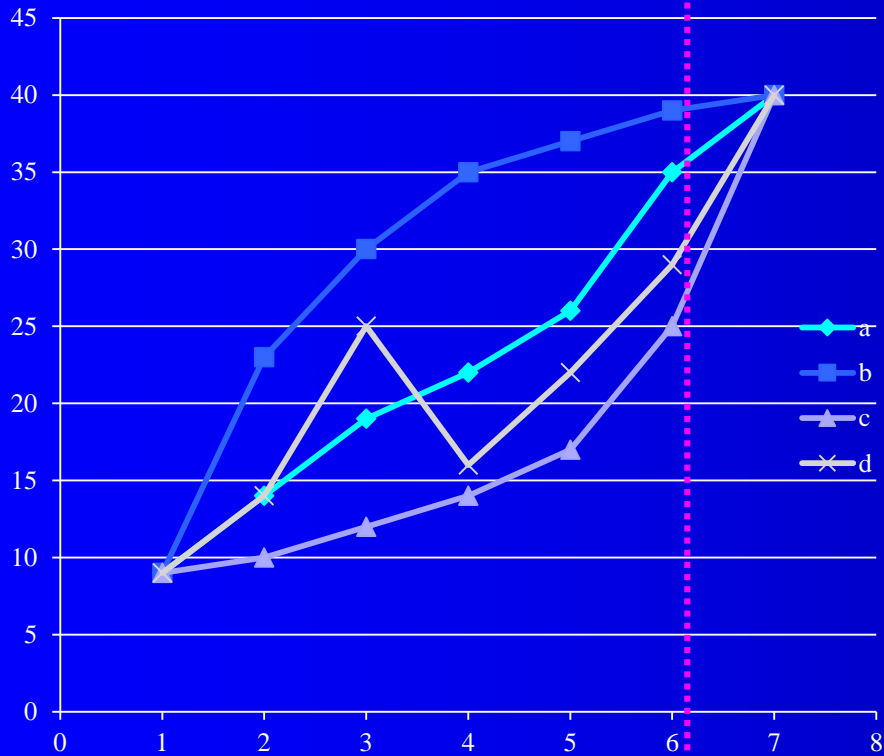
Families of adjacent pathways together make  
up a single connected grid.

# Mapping trajectories -exemplars

Recovery

Not everyone progresses past the dashed line: most plateau out.

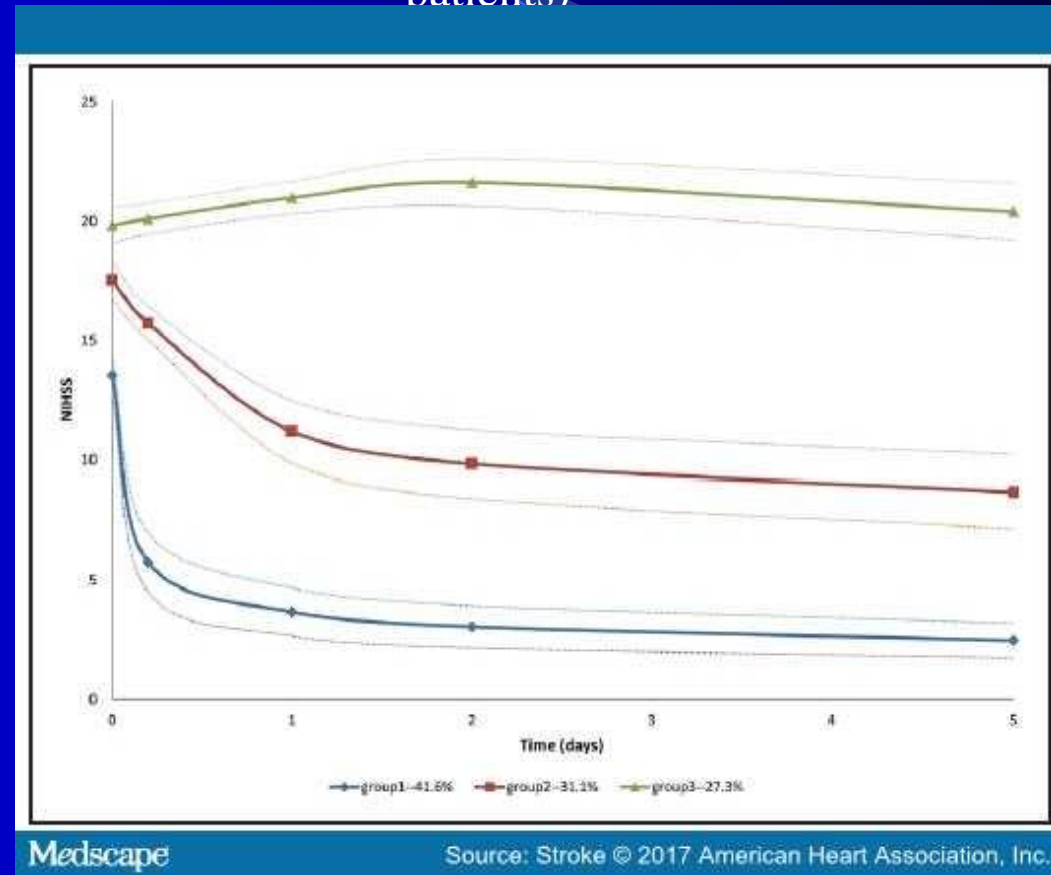
2d NIHSS (ESCAPE trial) and 90d mRankin (thrombectomy patients)



d1, wk1, mo1, mo2, mo3, mo6, yr1, yr5

Individual trajectories

Time



Medscape

Source: Stroke © 2017 American Heart Association, Inc.



# Brain Plasticity

**Potential:** Denotes the brain's capacity for anatomically implementing reactive changes in behavioural flexibility. (ability to change brain structure)

**Stimulus:** Prolonged mismatch between functional organismic supplies and environmental demands. (due to repeated external/environmental stimuli which the organism identifies it needs to react more effectively to in the future )

Example: Taxi drivers in London: (2000)

The hippocampus is a seahorse-shaped section in the vertebrate brain that is crucial for long-term memory and spatial navigation (rear section)

<https://www.scientificamerican.com/article/london-taxi-memory/>

There are multiple examples in everyday life: tennis coaching, online gamers, sim training – “Instinctive responses” – reduced reaction times with repetition.

# Plasticity – Peak periods

- Neuronal plasticity in the brain is greatly enhanced during critical periods early in life.
- Studies in primary sensory areas of the neocortex have revealed a substantial degree of plasticity in the mature brain.
- Plasticity in the adult neocortex lies dormant but can be reactivated by modifications of sensory input or sensory-motor interactions, which alter the level and pattern of activity in cortical circuits.
- Such interventions, potentially in combination with drugs targeting molecular brakes on plasticity present in the adult brain, might help recovery of function in the injured or diseased brain.

*Neuronal plasticity: beyond the critical period.*

*Cell.* 2014 Nov 6;159(4):727-37. doi: 10.1016/j.cell.2014.10.035.

# Rules of memory 'beautifully' rewritten

Engrams and circuits crucial for systems consolidation of a memory  
Episodic memories initially require rapid synaptic plasticity within the hippocampus for their formation and are gradually consolidated in neocortical networks for permanent storage.

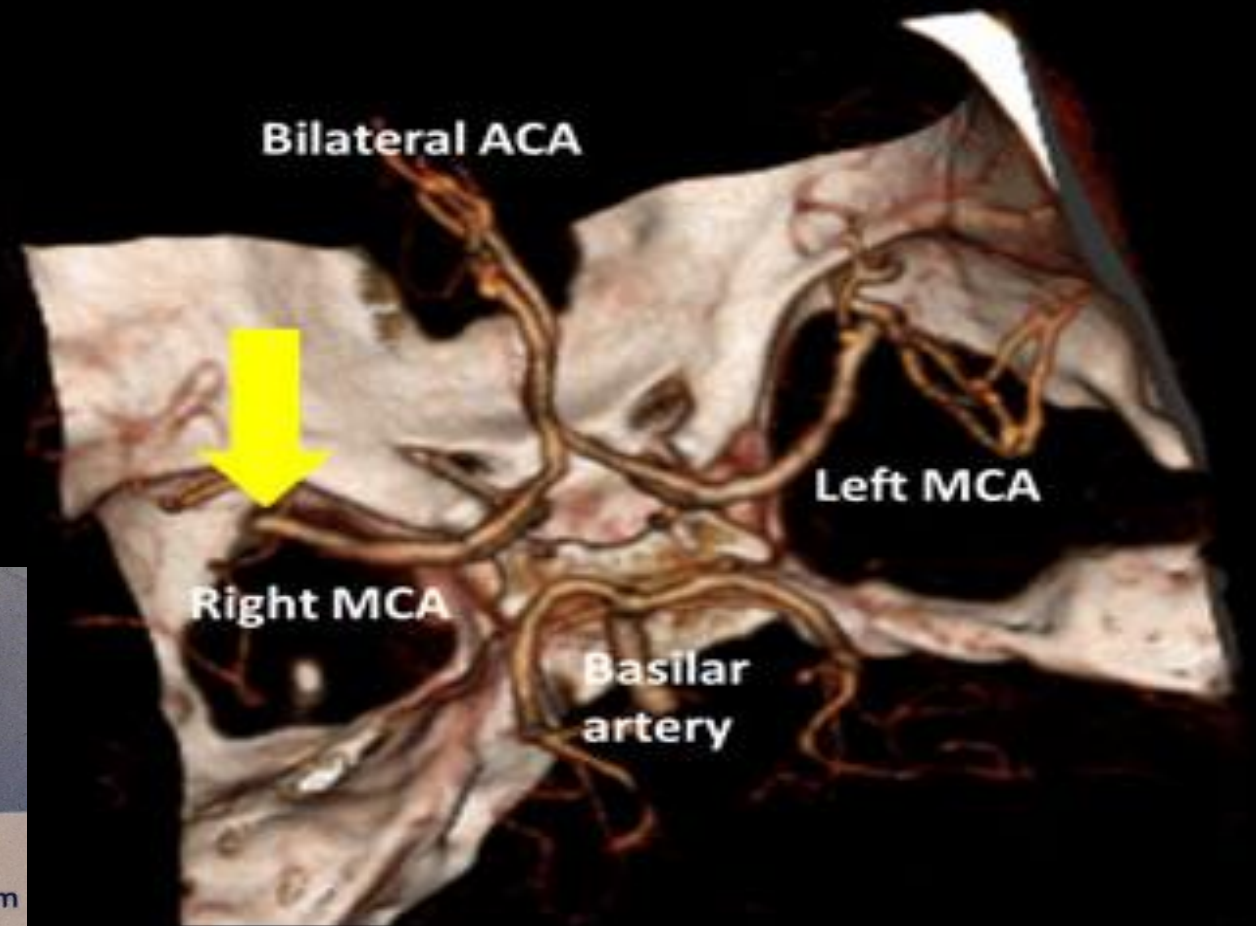
Hippocampal engram cells gradually became silent with time, engram cells in the basolateral amygdala, which were necessary for fear memory, were maintained.

The US and Japanese team found that the brain "doubles up" by simultaneously making two memories of events.

One is for the here-and-now and the other for a lifetime, they found.

It had been thought that all memories start as a short-term memory and are then slowly converted into a long-term one.

But – we're trying to reduce/avoid  
the need for "rehabilitation"



# THANK YOU

- Acknowledgements and restrictions:
- Images multiple sources including Personal, Radiopedia, NUTH patients, consultant colleagues, online google etc
- Information multiple sources - see individual slides
- Slides not to be used for financial gain.