put together by Alex Yartsev: Sorry if i used your image or data and forgot to reference you. Tell me who you are. aleksei.igorevich@gmail.com

~ Consider stroke ~
For any acute focal neuro deficit or any acutely altered consciousness

Cerebrovascular Accident

So, youre brought in by ambulance after falling over and becoming incoherent and incontinent…

History of Presenting Illness

When did it happen?? *Crucial for thrombolysis*

TIA and Stroke ONSET is ***ALWAYS SUDDEN***

Strokes usually happen ***IN THE MORNING***

There is usually ***NO PRECIPITATING EVENT*** *for stroke; haemodynamic TIA may result from a change in posture or strenuous activity*

BOX 5.3 Key points to elicit about focal neurological symptoms

1. Nature - Was the deficit of the motor, somatosensory, visual and/or other system?
2. Quality - Was there a loss of function (e.g. weakness or numbness) or a gain of function (e.g. jerking, parasthesiae)?
3. Anatomical distribution - For example, did the deficit involve the face, arm or leg, or the face, arm and leg?
4. Onset - Was it sudden, stuttering or gradual?
5. Evolution - For example, did the deficit recover, stabilise or proprogress?

Symptoms are ***FOCAL, NEGATIVE and MAXIMAL AT ONSET? = STROKE!!***

BOX 5.1 Focal neurological and ocular symptoms

Motor symptoms
Weakness or clumsiness of one side of the body, in whole or in part (hemiparesis)
Simultaneous bilateral weakness (paraparesis, quadriparesis)*
Difficulty swallowing (dysphagia)*
Imbalance (ataxia)*

Speech or language disturbances
Difficulty understanding or expressing spoken language (dysphasia)
Difficulty reading (dyslexia) or writing (dysgraphia)
Difficulty calculating (dyscalculia)
Slurred speech (dysarthria)*

Sensory symptoms

Somatosensory
Altered feeling on one side of the body, in whole or in part (hemisensory disturbance)

Visual
Loss of vision in one eye, in whole or in part (transient monocular blindness or amaurosis fugax)
Loss of vision in the left or the right half or quarter of the visual field (hemianopia, quadrantanopia)
Bilateral blindness
Double vision (diplopia)*

Vestibular symptoms
A spinning sensation (vertigo)*

Behavioural or cognitive symptoms
Difficulty dressing, combing hair, cleaning teeth, etc.; geographical disorientation; difficulty copying diagrams such as a clock, flower or intersecting cubes (visual–spatial–perceptual dysfunction)
Forgetfulness (amnesia)*

* As an isolated symptom, this does not necessarily indicate transient focal cerebral ischaemia, because there are many other potential causes.

BOX 5.2 Non-focal neurological symptoms

Generalised weakness and/or sensory disturbance
Lightheadedness
Faintness
'Blackouts' with altered or loss of consciousness or fainting, with or without impaired vision in both eyes
Incontinence of urine or faeces
Confusion
Any of the following symptoms, if isolated*

- A spinning sensation (vertigo)
- Ringing in ears (tinnitus)
- Difficulty swallowing (dysphagia)
- Slurred speech (dysarthria)
- Double vision (diplopia)
- Loss of balance (ataxia)

* If these symptoms occur in combination, or with focal neurological symptoms, they may indicate focal cerebral ischaemia.

Is your patient very OLD?? *90% of strokes happen to* ***!! over55s !!***

TIA differs only in duration:
resolves
in 24 hrs

TABLE 5.1 Neurological symptoms during transient ischaemic attacks[1]

	Proportion*
Unilateral weakness, heaviness or clumsiness	50
Unilateral sensory symptoms	35
Slurred speech (dysarthia)	23
Transient monocular blindness	18
Difficulty speaking (dysphasia)	18
Unsteadiness (ataxia)	12
Dizziness (vertigo)	5
Homonymous hemianopia	5
Double vision (diplopia)	5
Bilateral limb weakness	4
Difficulty swallowing (dysphagia)	1
Crossed motor and sensory loss	1

* Percentage of 184 - the proportion of patients with TIA with various focal neurological symptoms from the Oxfordshire Community Stroke Project; many patients had more than one symptom (e.g. weakness as well as sensory loss) and no patient had isolated dysarthria, ataxia, vertigo, diplopia or dysphagia.

Symptoms and signs in the diagnosis of stroke

Like the diagnosis of TIA, the diagnosis of stroke is also clinical and depends crucially on an accurate history, taken from the patient, carer or witness. To decide whether the symptoms and signs are due to a vascular event of the brain, ensure that:

- The neurological symptoms and signs are focal (i.e. neuroanatomically localising) rather than non-focal
- The focal neurological symptoms are negative in quality (i.e. loss of function) rather than positive (i.e. muscle paralysis rather than jerking, numbness rather than pins and needles, blindness rather than visual hallucinations)
- The onset of the focal neurological symptoms was sudden
- The focal neurological symptoms were maximal at onset (i.e. evolving over minutes in all of the affected body parts) rather than progressive (evolving over hours to days, and migrating from one body part to another).

Symptoms indicating a TIA

The diagnosis of TIA is clinical, and rests on the description by the patient or an eye-witness of symptoms:

- of *loss* of *focal* neurological or monocular function (*see Table 5.1*)
- of *sudden onset*
- that are *maximal at onset*, without spread or intensification
- that are thought to be due to *inadequate blood supply* to the brain or eye as a result of arterial thrombosis or embolism, associated with disease of the arteries, heart of blood
- that resolve within 24 hours.

Risk of stroke doubles for every decade after 55 y.o.

ALSO ask about risk factors: AGE?
1st degree relatives? Hypertension? Cholesterol? Smoking??
Diabetes? Heart disease, esp. Atrial Fibrillation? Homocysteinaemia? Prior strokes?- 14% recur in 1 yr!

STROKE SYNDROMES by VASCULAR TERRITORY

Middle Cerebral Artery: Total occlusion

CONTRALATERAL HEMI-EVERYTHING

-plegia, -anopia, -anaesthesia; DOWN TO THE THE HIP

taken out sensory and motor cortex, damaging the optic tract with oedema

eyes and head deviate towards the side of the lesion

PLUS either DOMINANT or NON-DOMINANT symptoms:

Global aphasia: complete failure of comprehension and expression

Anosognosia, hemineglect, constructional apraxia

ANTERIOR CEREBRAL ARTERY: the Seat of Manners

BEHAVIOURAL ABNORMALITIES:

- Paucity of insight., slowness of thought, apathy, distractability

usually happens when you congenitally have both ACAs arising from one stem; this way you infarct bilaterally

+ CONTRALATERAL FOOT, LEG and GENITAL FAILURE:

Hemiplegia and hemianaesthesia sparing the upper limbs and face (therefore also INCONTINENCE)

MCA Superior division

WEAKNESS of UPPER LIMBS and FACE

(so called "Brachiofacial paralysis")

BROCA'S EXPRESSIVE APHASIA and / or DYSARTHRIA

The DOMINANT MCA allows

LANGUAGE and ART

Thus: stroke out here, and its

APHASIA and APRAXIA for you

MCA Inferior Division

CONTRALATERAL HEMIPLEGIA

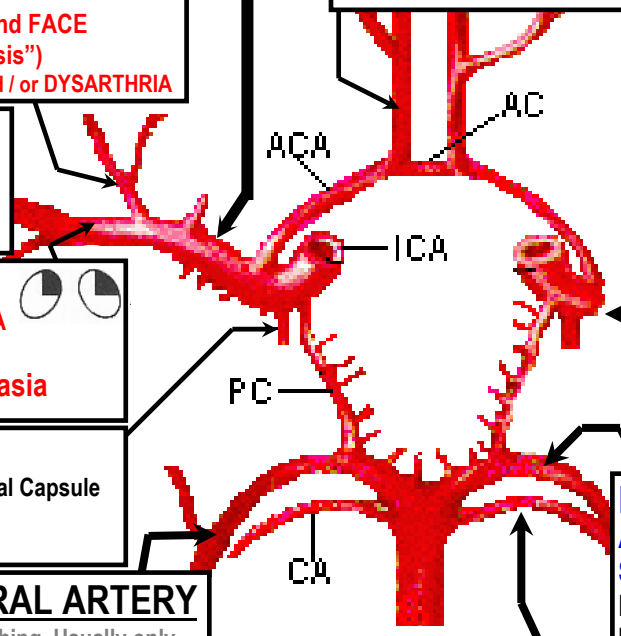
SUPERIOR QUADRANTINOPIA

Wernicke's Receptive Aphasia

Anterior Choroidal

Supplies Posterior Limb of Internal Capsule and lateral geniculate Nucleus

HEMIPLEGIA AND HEMIANOPIA



The NON-dominant MCA: WEIRDNESS

In the Superior division:

...Brachiofacial paralysis, as well as

Anosognosia: you stubbornly fail to notice that you have a serious neurological deficit

Hemineglect: everything on that side does not exist for you, you just ignore it

Constructional apraxia: inability to mentally rotate objects, follow maps, copy pictures

Dressing apraxia: unable to operate simple shirts

In the Inferior division:

...Superior Quadrantinopia, as well as

APROSODIA (inability to perceive the emotional content of speech)

Non-Dominant PCA stroke:

Anomia for familiar faces (prosopagnosia)

Spatial Disorientation

BILATERAL TEMPORAL PCA STROKE:

Hippocampus damaged, thus PERMANENT AMNESIA

POSTERIOR CEREBRAL ARTERY

Rarely will you infarct the whole thing. Usually only one of the branches:

VISUAL DISTURBANCE eg.

Homonymous hemianopia with macular sparing

HEMIBALLISMUS if subthalamic nuclei infarcted

IN THE DOMINANT HEMISPHERE:

ANOMIA, AGNOSIA, ALEXIA in occipitotemporal stroke

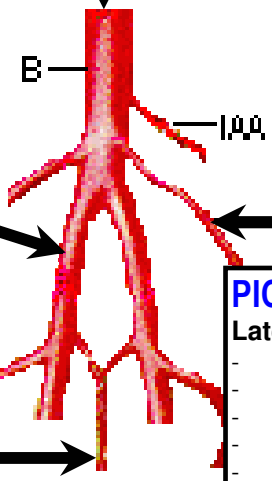
BASILAR ARTERY OCCLUSION:

"locked-in syndrome"

complete paralysis with preservation of consciousness almost uniformly fatal

Superior Cerebellar:

- ipsilateral limb and gait ataxia
- Horner's syndrome
- tremor
- contralateral limb dysmetria
- contralateral loss of pain and temperature sensation over the body and face,
- loss of limb position sense
- DEAFNESS



AICA: Pontine Infarct

- **DEAFNESS**
- **loss of pain and temperature sensation on the face AS WELL AS complete paralysis of the face;**
- **Ipsilateral limb and gait ataxia**
- **Dizziness**
- **Nystagmus**

VERTEBRAL ARTERY OCCLUSION:

What happens depends on the quality of your other vertebral artery: if you don't have one, this has the effect of a basilar artery stroke.

Anterior Spinal Artery: Medial Medullary Syndrome

weakened tongue on the affected side

(due to involvement of the hypoglossal nerve),

weakness of the contralateral limbs

Decreased position and vibration sense

PICA: Lateral Medullary Syndrome

Lateral medullary syndrome;

- Dysarthria
- Dysphagia
- Dysphonia
- Vertigo
- Nystagmus
- Ataxia or Unsteady gait
- Loss of taste and paralysis of the palate

Loss of pain + temperature: IPSI face- CONTRA body

Ipsilateral Horner's Syndrome

Mimicking Stroke:

The most frequent stroke mimics include
seizures (17%);
systemic infections (17%);
brain tumors (15%);
toxic-metabolic causes,
such as hyponatremia (13%);
positional vertigo (6%).

REMEMBER:
Hypoglycaemia
Head trauma
Brain Tumour
Epilepsy
Hemiplegic migraine
Syncope
TIA
Meningitis

Miscellaneous disorders
- **syncope,**
- **trauma,**
- **subdural hematoma,**
- **herpes encephalitis,**
- **transient global amnesia,**
- **dementia,**
- **demyelinating disease,**
- **myasthenia gravis,**
- **parkinsonism,**
- **hypertensive encephalopathy,**

Examination: Where did the clot come from?

ATRIAL FIBRILLATION? ENDOCARDITIS? Then, peripheral vascular system:
- carotid auscultation for bruits,
- blood pressure, and pressure comparison between arms
- examine extremities for ischaemia (peripheral emboli),
- retina [effects of hypertension and cholesterol emboli (Hollenhorst plaques)];

PLUS: look for signs of head trauma

Its all about the BRUITS

Investigate bruitts with DOPPLER ultrasound

Tests and Investigations

WITHIN 24 HOURS: to distinguish haemorrhage from infarct

CT scan of the BRAIN: → ..CT again each time they deteriorate

CT excludes 90% of intracranial haemorrhages; the other 10% can be picked up with LUMBAR PUNCTURE
by12 hours after a subarachnoid bleed, blood breakdown products collect at the base of the spine, and can be drained for analysis – you are looking for **XANTHOCHROMIA,** or yellowness

Exclude non-Vascular Causes! Eg. tumour

Confirm infarction: if its visible yet: an infarct of the brain takes hours to ripen, and even after 3 hours the changes are very subtle

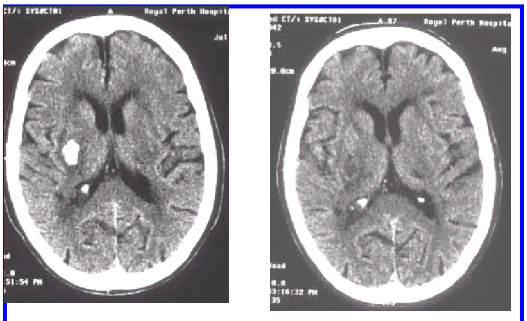
- **Rule out intracerebral haemorrhage and sub-arachnoid bleeding:**
Whitish areas, especially in the base of skull;
Subarachnoid → the CSF in the ventricles will be bright, it is mixed with blood
done within the first few days of stroke, CT identifies
  - **intracerebral haemorrhage in all cases,**
  - **SAH in about 95-97% and**
  - **cerebral infarction in about two-thirds.**

CT will miss little infarcts, early infarcts, posterior fossa infarcts (obscured by artefacts)

NOTE: A CT scan done too early (before oedema begins) **will yield nothing !!**
thus, **a NORMAL CT DOES NOT EXCLUDE A STROKE!!**
But… even 5 hrs after the CVA the CT will give findings in 50% of cases
So scan anyway, just to have a baseline picture of their brain

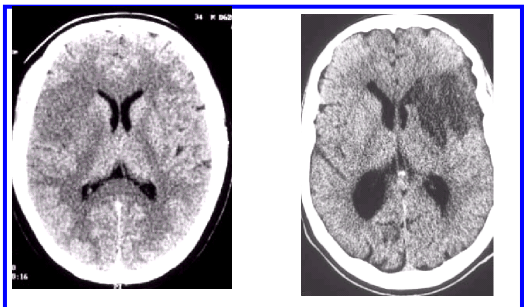
WHAT ARE YOU LOOKING FOR?

The evolution of a haemorrhage:
- **Immediately:** a white, hyperdense area
- **Within days:** becomes less dense (turns to clot)
- **after a few days to a few weeks** (depending on its size) it becomes isodense with surrounding brain tissue ('fogging') and may be difficult to see.
Smaller haemorrhages fog up faster
- **Thereafter** the haemorrhage becomes hypodense and may be mistaken for an old infarct



Intracranial haemorrhage: same pt, 14 days apart; note the darkened spot which is all that remains of the haemorrhage in the right. posterior putamen

The evolution of an infarct:
hyperacute stage : the CT image often appears normal.
Sometimes might find a **hyperdense artery** (see the **thrombus** in it)
within 3 hours there are usually subtle changes in the ischaemic brain
= loss of normal grey-white matter differentiation
= **compression of the lateral ventricle** due to focal brain edema
= and **hypodensity!!** Dark greyness…
during the first few days,
becomes more clearly demarcated and well defined
and more hypodense (black)
around days 3–5 the swelling of the infarct is usually maximal
during the second and third week the swelling subsides
Eventually a sharply demarcated, atrophic, hypodense (similar to CSF) defect remains: the INFARCT CAVITY



Early stroke: greyish *Old stroke (blackish)*

MRI for stroke:

Diffusion Weighted Imaging is much more helpful than CT in the early phase

Infarcts of any size are more often and more quickly visible

However, even MRI can be normal in a clinically definite stroke !!

Minutes: loss of the normal flow void in the symptomatic artery within minutes of onset
(the MR equivalent of the hyperdense artery sign on CT)
3 hours: swelling of the ischaemic brain on T1-weighted images, but without signal change on T2-weighted images
8 hours: signal changes on T2-weighted images
16 hours: signal change on T1-weighted images.
Large infarcts are often visible on routine T1- and T2-weighted imaging within 6 hours,
… but small cortical and subcortical infarcts may never become visible.

Also may want to consider Magnetic Resonance Angiography

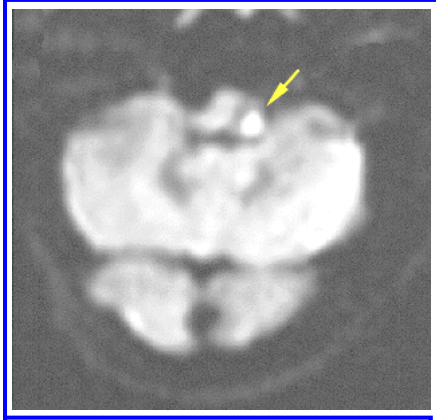
The advantages of MRI over CT are:

1. Better soft tissue contrast resolution;
2. Multiplanar capabilities;
3. No ionising radiation;
4. No bone artifacts which limit the sensitivity of lesion detection in the posterior fossa;
5. Very sensitive to changes in water concentration in tissues and therefore superior detection of lesions; and
6. Ability to perform both anatomic and physiological imaging.

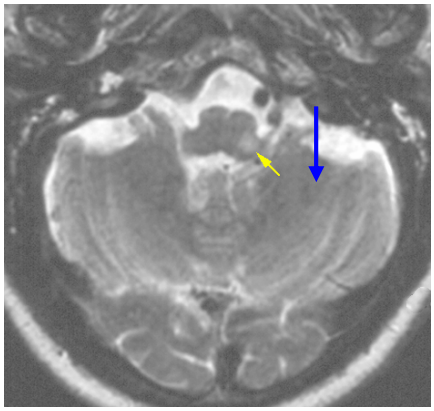
The disadvantages of MRI are:

1. More expensive than CT (between two and three times more);
2. Less accessible to patients because there are less units than CT in Australia;
3. Problems with cardiac pacemakers and other implants including aneurysmal clips; and
4. Claustrophobia

MRI has not been evaluated for
(and is generally held to be useless at)
picking up very acute haemorrhage



Diffusion-weighted MRIs are good at showing cytotoxic edema, which appears as a hyperintense (white) region. This edema is seen in infarcts that are aged from a few hours to 10 days. In this image, a hyperintense region is seen in the left lateral medulla (arrow), indicating an acute infarct in this region. The resolution of diffusion-weighted images is not as good as T1 or T2 images, but their advantage is that they can show very early infarcts.



T2 MRI
In T2 MRIs the CSF is white. In this MRI performed 3 days after a stroke a hyperintense (pale) region is seen in the left lateral medulla (arrow) oblongata. This represents edema within an area of infarction.

OTHER INVESTIGATIONS:

FBC, ESR: looking for infectious WBC changes
urea, creatine, electrolytes: looking for renal disease 2ndary to renal artery stenosis (comorbid with hypertension)
Liver Function Testing: looking to exclude hepatic encephalopathy
Random Glucose: looking to exclude ketoacidosis coma
Serum cholesterol & triglycerides looking for hyperlipidaemia (a risk factor)
Chest X-ray looking for signs of heart failure, in particular LV and LA enlargement
ECG: looking for signs of dysrhythmia, in particular atrial fibrillation
Echocardiogram: looking for atrial appendage clots and septal defects
Lumbar Puncture to support a diagnosis meningitis if that's what it looks like
Echo doppler : looking for carotid stenosis and/or aneurism, even if there wasn't a bruitt.

How is this diagnosis made ?

By CT, MRI, and the exclusion of hypoglycaemia, infection, trauma and tumour

MANAGEMENT

Immediately:

CIRCULATORY AND RESPIRATORY SUPPORT:

Make sure they have an airway and are saturating

Make sure they are not dehydrated

REPLACE FLUIDS INTRAVENOUSLY: NIL BY MOUTH until cleared as somebody who can swallow without choking.

Is the ICP RISING? you don't know!

→ insert an ICP monitor IF:

- Glasgow score 8
- Midline shift on CT
- massive subarachnoid bleed
- brain stem compression

If CT scan excludes haemorrhage, aspirin (150-300mg) should be given as soon as possible

ARE THEY PERFUSING THEIR BRAIN?

Whats their cerebral perfusion pressure?

If you know their Intra Cranial Pressure and their Mean Arterial Pressure…

CPP = MAP – ICP

The normal ICP should be less than 20 mmHg and the normal CPP should be more than 60 mmHg.

WATCH THEIR BLOOD PRESSURE: mainly out of morbid interest

Give them more fluids if they are hypotensive, BUT-

DO NOT attempt to lower even ridiculously high blood pressures:

High blood pressure helps perfuse the highly stenosed brain vessels

THUS wait 7 – 10 days before staring new antihypertensives

HOWEVER if they are already on anti-HT meds, **YOU CAN FEED THEM THEIR OWN PILLS** …carefully watching their blood pressure and monitoring them for signs of deterioration.

Dexamethasone is NOT INDICATED for the treatment of strokeish ICP elevation

IF THE SYSTOLIC IS OVER 220, lower their blood pressure: that way they will become eligible for thrombolysis.

Use a short-acting drug which has a reduced effect on intracranial vessels, eg. LABETALOL (Alpha-Blocker and nonselective beta-blocker)

KEEP ICP BELOW 20

How this is done is detailed in the management of brain injury in the ICU.

Essentially you sedate them, straighten their neck, raise their BP to maintain CPP, give loop diuretics, mechanically hyperventilate, give mannitol or IV glycerine, or decompress surgically with ventricle drain or craniotomy.

ESTABLISH NORMOGLYCAEMIA

Thrombolysis

ONLY in the 1st 3 hours

ONLY for major severe strokes

ONLY if you have excluded a bleed

ONLY intravenous tPA

ONLY in the hands of people trained in its use.

NEVER in uncontrolled hypertension (not over 185 systolic)

NEVER in thrombocytopenic patients

RISK OF FATAL BLEED = 1 in 16

ADMINISTER NEUROPROTECTIVE DRUGS

- **May be medicolegal suicide, as none have been proven to have a measurable effect on survival;**

ANTICOAGULATE with heparin

- **if particularly keen; but 1-4% of patients with stroke will upgrade to hemorrhagic stroke when anticoagulated (i.e the clot you dissolved was holding the blood in a vessel somewhere)**

PLUS: may consider anticoagulation if the patient is looking at a prolonged hospital stay

Long-Term Rehabilitation:

Administer therapy to address those functions lost as the result of CVA:

Eg.
SPEECH THERAPY
OCCUPATIONAL THERAPY
PHYSIOTHERAPY
COUNCELLING
PSYCHOTHERAPY

STROKE UNIT is the best place to recover from a CVA because its swarming with the abovementioned specialist allied health staff

Most people stay for months…

Key words to spout in the barrier: "Therapeutic Alliance" and "Multidisciplinary Team Approach"

Prognosis

Stroke is the **third leading cause of death and the leading cause of disability in the US.**
Cerebrovascular disease was the **second leading cause of death worldwide** in 1990, killing over 4.3 million people.
Cerebrovascular disease was also the **fifth leading cause of lost productivity**

Epidemiology

In the US: Incidence for first-time strokes is more than 400,000 per year.
At current trends, this number is projected to jump to **one million per year by the year 2050.**

Risk factors:

Risk factors you cannot change

- **Age.** Nine out of ten strokes affect people over 55.
  The risk for stroke increases with age.
  The risk doubles every decade you are over 55.
- **Race.** African-Americans and Hispanics have 2 to 3 times the risk of ischemic stroke
- **Gender.** Stroke is more common in men than women.
  However, at older ages, more women than men have strokes.
  At all ages, more women than men die of stroke.[2]
- **Family history.** The risk for stroke is greater if a parent, brother, or sister has had a stroke or TIA.
- **Prior history of stroke or TIA**.
  About 14% of people who have a stroke have another stroke within 1 year.[2]
  Up to 25% have another stroke within 5 years.[3]

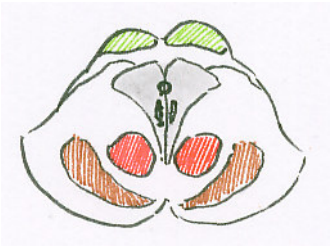
Risk factors that you can change

- **Hypertension** = the second most important stroke risk factor after age.
- **Diabetes.** About one-quarter of people with diabetes die of stroke.
  Having diabetes **doubles your risk** for stroke
- **High cholesterol**.
- **Other heart conditions** such as atrial fibrillation, endocarditis, heart valve conditions, and cardiomyopathy
- Other diseases : lupus, syphilis, hemophilia, pneumonia, high levels of homocysteine, and periodontal disease.

Pathophysiology

CAUSES OF COLLAPSE

= either with retention of consciousness or with loss of consciousness.
=Loss of consciousness =
EITHER cerebral cortex has been disturbed diffusely,
OR that the **Brainstem Reticular Formation**



Common causes = ***epilepsy***

- tonic-clonic,
- absence,
- akinetic

Recovery is usually rapid, though some patients may carry on having continuous seizure (status epilepticus).

cerebrovascular disease
especially if the reticular formation is involved in a **brain stem stroke or in massive cerebral strokes such as subarachnoid hemorrhage**.
The collapse is usually of **longer duration** than in syncope or epilepsy

syncope - a sudden and brief loss of consciousness associated with a loss of postural tone, from which recovery is spontaneous.
ALL SYNCOPE = result of DECREASED CEREBRAL OXYGENATION

... **Syncope can be**

1. **neurally mediated (vasovagal syncope)**
   = reflex-mediated changes in vascular tone or heart rate. This is the commonest cause of syncope, and may be due to emotional factors or activation of receptors in organs such as the bladder (micturition syncope) or the carotid sinus.
2. **orthostatic hypotension**
   (volume depletion, medications, primary and secondary – e.g. diabetes - autonomic failure).
3. **psychiatric** (e.g. panic attacks).
4. Due to **primary cardiac** conditions such as **structural heart diseases (such as aortic stenosis) or arrythmias**.

*In about a third of cases a **cause cannot be found.***

CEREBRAL ISCHAEMIA

- **The blood flow to the brain is controlled relatively independently to that of the rest of the body.**

VASCULAR CONTROL

!! CRITICAL NEED FOR STABLE PREESSURE !! →
REMAINS CONSTANT for 50 – 150 mmHg
This is known as **cerebral autoregulation** .
(increased pressure = dilation of arterioles to drop the pressure)

METABOLIC CONTROL

increase in the partial pressures of CO_2 (pCO_2) = vasodilation,
decrease in pCO_2 = vasoconstrictor.

THUS: sudden and local changes to blood flow, matching neurone activity.
Increased local neural metabolic activity
→ the release of CO_2 (which leads to a decrease in local pH)
→ local vasodilation.
→ increased blood flow
→ Thus, need for more nutrition is met

Cerebral blood flow is also controlled by both sympathetic and parasympathetic autonomic nerves.

sympathetic = from the **superior cervical ganglion** in the neck,
Parasympathetic = from seventh (**facial) cranial nerve.**
→ **IMPORTANT ROLE UNDER ABNORMAL CIRCUMSTANCES**

eg. SYMPATHETIC : extremes of pressure autoregulation (when b.p. approaches 50 or 150)
PARASYMPATHETIC: **dilating vessels** under conditions of **focal hypoxia or ischaemia**
THUS; AUTONOMIC REGULATION = DAMAGE CONTROL

COMPROMISED BLOOD SUPPLY IS DUE TO:

- blockage or rupture of an artery
- blockage of a vein.
- a severe fall in arterial blood pressure

less severe hypotension causes decreased perfusion at sites of potential limited cerebral circulation

→ leads to "boundary/watershed zone" infarcts between the territories of, for example, the anterior and middle cerebral arteries. If the reduction of blood supply is of brief duration (e.g., migraine or tranisient ischaemic attack) full recovery of neural function is the rule.

If reduction in blood supply is **prolonged enough to cause ischaemic necrosis (i.e. infarction) very little recovery of neural tissue function can be expected**.

Following a stroke, arterial pressure is often elevated.
However, there is usually severe disruption to normal autoregulatory mechanisms of cerebral blood flow.

Giving agents that lower arterial pressure, therefore, may seriously compromise cerebral perfusion.

CAUSES OF STROKE **6.01**

stroke = prolonged neurological deficit with sudden onset and a vascular basis.
Transient ischaemic attacks = short-term neurological deficit that resolves quickly.

Take history and examine to determine:
1. What is the cause of this patient's stroke?
2. Is there effective therapy for this stroke?
3. Can the chance of a further stroke be reduced?

Strokes can be due either to **OCCLUSION** (→ ischaemic necrosis; infarction)
Or **RUPTURE** (→ haemorrhage)

INFARCT:

MOST OFTEN:
cause of infarct is **atheroma in the internal carotid** artery near its origin from the common carotid artery.
ALSO atheroma may form
at the **termination of the internal carotid artery** and in the **basilar artery.**

Small embolus = only TIA, and more commonly to deep structures.

Small penetrating arteries to the deep parts of the brain can be occluded by atheroma, thrombus, or hypertensive thickening of the vessel walls.
THUS, small infarcts will be found in the deep structures of the brain such as the basal ganglia

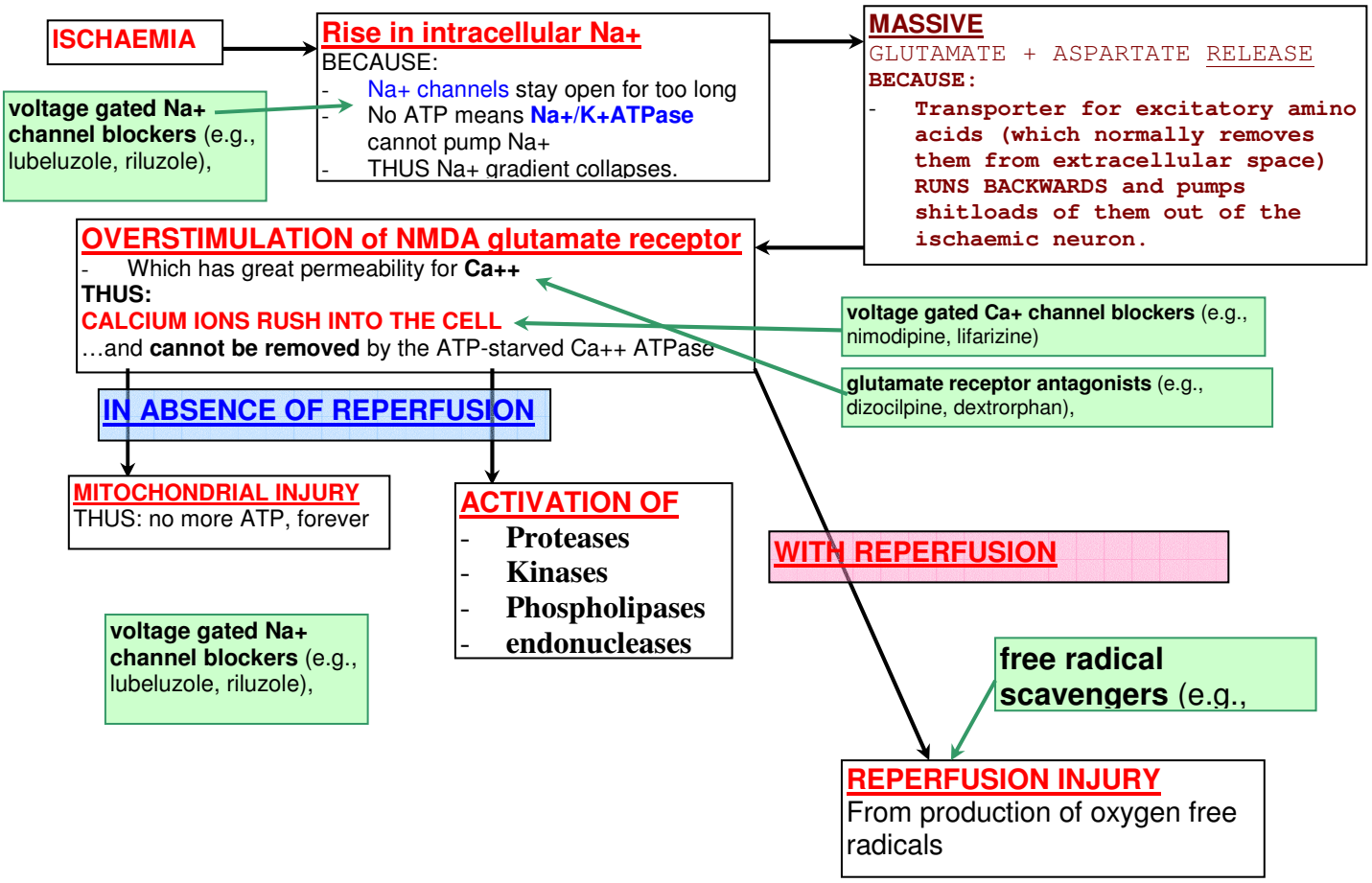
HAEMORRHAGE:

usually due either to
1. **rupture of a berry aneurysm** at the base of the brain,
- giving rise to a **subarachnoid hemorrhage,**
2. **rupture of a small penetrating artery**
- gives rise to a hematoma deep in the brain (an intracerebral hemorrhage).
- These have become less common with better control of arterial hypertension.

NEUROPROTECTIVE AGENTS *6.01*

NORMALLY: treat stroke by addressing thrombogenesis or thrombolysis.
Eg: heparin, aspirin, tPA
NO LONGER!! Noveau therapies aim at cellular disturbances of ischaemia

PATHOLOGY OF BRAIN INFARCTION:



Neuroprotective agents act by targeting one or more of these abnormal cellular events.
these drugs target the peri-infarct area which lies between the non-salvageable, ischaemic core and normally perfused brain.

The peri-infarct area is thought to be recruited into the infarcted core over several hours **(evolving stroke),** providing a therapeutic window for drug intervention.

Thus, it is hoped that neuroprotective agents will prevent "at risk" tissue progressing to infarction, thereby reducing brain damage caused by stroke.

They include
glutamate receptor antagonists (e.g., dizocilpine, dextrorphan),
voltage gated Na+ channel blockers (e.g., lubeluzole, riluzole),
voltage gated Ca+ channel blockers (e.g., nimodipine, lifarizine)
free radical scavengers (e.g., tirilazad).

PHARMACOLOGY OF ASPIRIN *6.02*

Aspirin (acetylsalicylic acid) = COX enzyme system inhibitor.

This enzyme system, now called cyclo-oxygenase, converts arachidonic acid to products such as prostaglandins (PGs) and thromboxane (Tx). The major arachidonic acid metabolite in platelets is thromboxane A2, which is proaggregatory and the major metabolite in endothelial cells is prostacyclin(PGI_2) which inhibits platelet aggregation.

Aspirin acetylates many proteins, binding to them irreversibly. In the case of platelet cyclo-oxygenase, this irreversible binding **inhibits thromboxane synthesis for the lifespan of the platelets.**

Thus, prolonged bleeding tendency will last for several days after cessation of treatment with aspirin.

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long-term treatment with aspirin reduces the incidence of cerebro-vascular events in patients with previous strokes or transient ischaemic attacks.

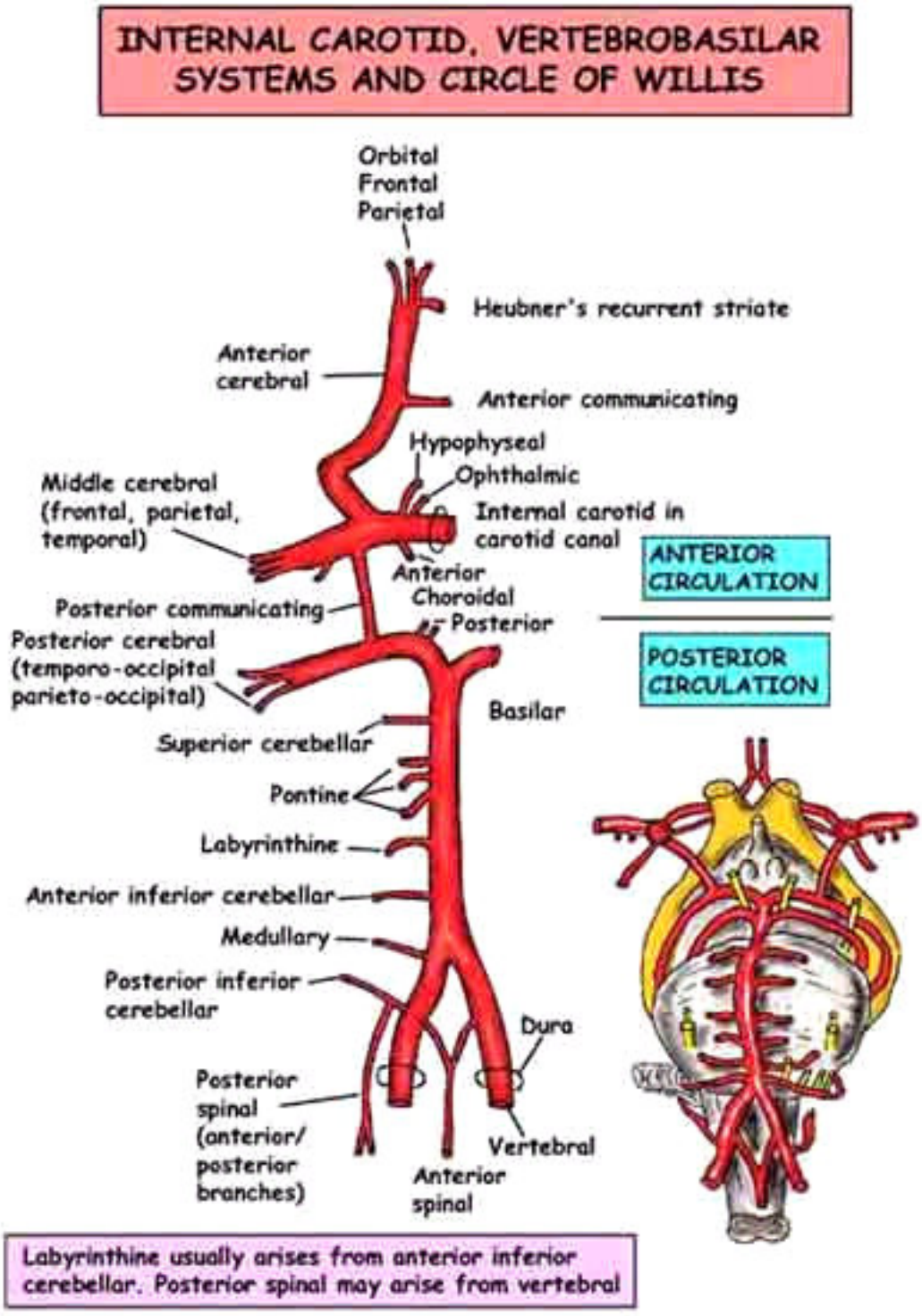
Clinical studies in normal volunteers suggested that low doses of aspirin (less than 100 mg) effectively inhibit platelet cyclooxygenase activity with only slight inhibition of vessel wall PGI_2 formation.

daily doses of 30 mg aspirin are no less effective than 283 mg
and the lower dose has less side effects (Dutch TIA Trial, 1991).

Therefore:

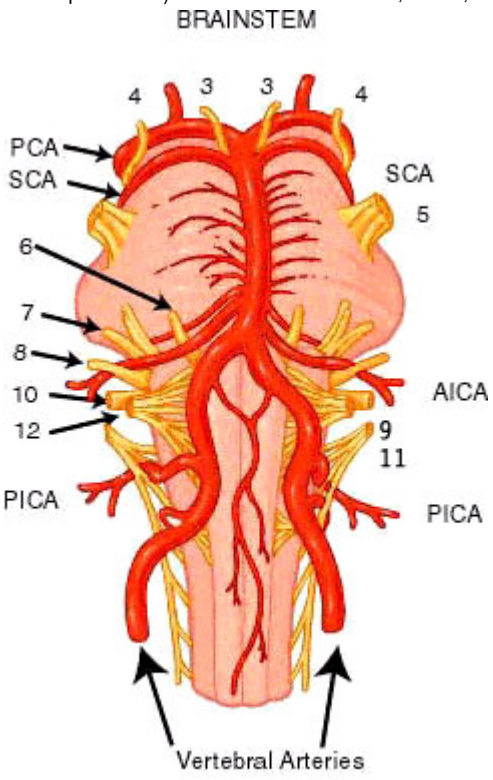
use aspirin (in doses of 100-300mg/day) in patients needing secondary prevention of cerebrovascular disease provided that there are no contraindications (Orme, 1988).

Relevant anatomy



In the medulla, as in the spinal cord, the different fibre tracts are segregated from each other. For example, the corticospinal tracts are found within the pyramids lying ventrally in the medulla; the dorsal spinocerebellar tracts are found within the inferior cerebellar peduncle located dorsolaterally; the medial lemnisci are found close to the midline, and the spinothalamic tracts are found laterally. Two major decussations occur in the medulla. First, the huge pyramidal (corticospinal) decussation which defines the caudal boundary of the closed medulla, and second, the sensory decussation of the axons from the gracile and cuneate nuclei, located more rostrally in the closed medulla.

The reticular formation of the medulla is made up of many distinct groups of cells concerned with specific functions, the majority of which, are crucial for the maintenance of life. For example, the reticular formation contains small cell groups regulating cardiovascular function, and other autonomic activities, as well as respiration. The reticular formation carries out these critical functions, in part, by controlling directly the activity of the spinal cord (e.g., via reticulospinal tracts). The reticular formation is, in turn, under the control of higher centres.]



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The brain receives its vascular supply from the internal carotid and vertebral-basilar arterial systems. The internal carotid arteries predominantly supply forebrain structures, while the vertebral-basilar system supplies the cervical spinal cord, brainstem, cerebellum, occipital and portions of temporal neocortex. The two systems meet and anastomose in the circle of Willis on the ventral surface of the brain. This has important clinical implications. For example, if a proximal artery (e.g., the internal carotid artery) is occluded, blood flow to a distal branch (e.g., the anterior cerebral) may be supplied from the other major arteries contributing to the circle.

The vertebral-basilar arterial system has many branches. The most important are the posterior inferior cerebellar artery (PICA), the anterior inferior cerebellar artery (AICA), the superior cerebellar artery (SCA) and the posterior cerebral artery (PCA). Many of the branches of the vertebral-basilar arteries that supply the brainstem also supply the cerebellum (e.g. PICA, AICA and SCA).

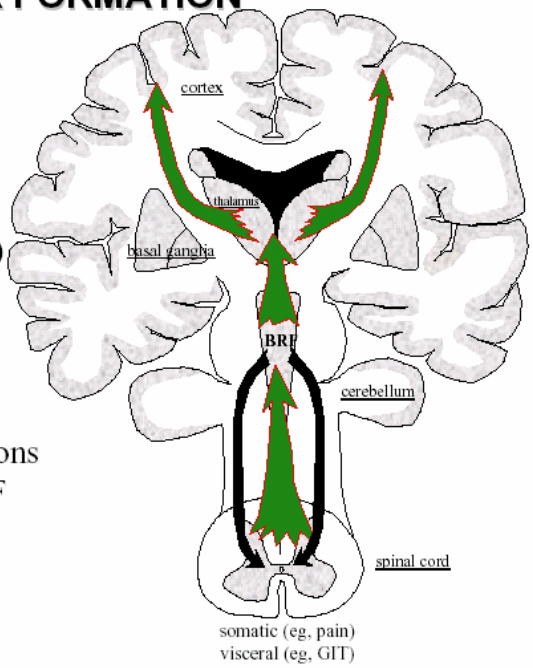
In the brainstem, the zone of supply of each arterial branch of the vertebral artery is characteristically "wedge-shaped". For example, in the caudal medulla, three wedges of supply are seen on each side. The most lateral wedge is supplied by the posterior inferior cerebellar artery, the middle wedge is supplied by the vertebral artery itself, and the most medial wedge is supplied by the anterior spinal artery. Thus a blockage of an individual artery will cause a distinctive wedge-like zone of infarction in the medulla, and this will be manifest as a distinct set of symptoms and signs which can be recognised on clinical examination.

BRAINSTEM RETICULAR FORMATION

* primitive core

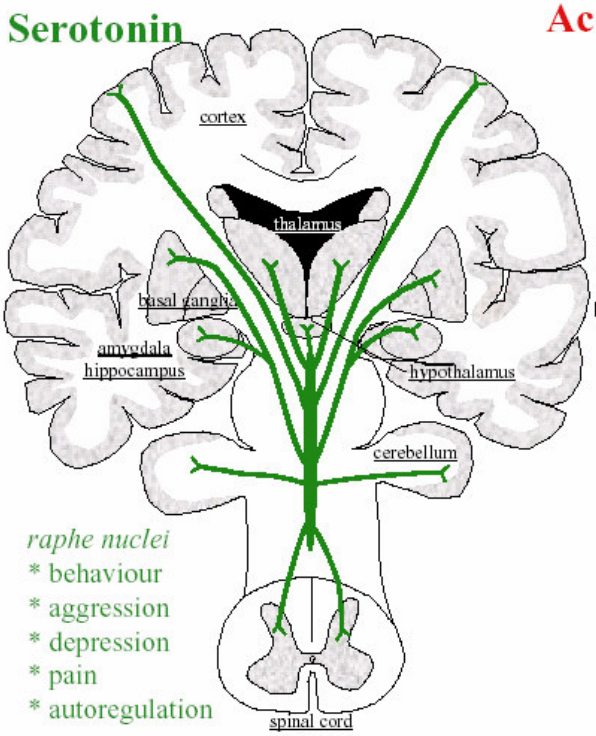
* 2 general functions (related)
(i) **Arousal-Mood Setter**
- samples somatic/visceral worlds
- sets forebrain activity (arousal/mood)
(ii) **Autonomic Policeman**
- monitors somatic/visceral world
- influences crucial reflexes

* individual nuclei with distinct functions
* neurotransmitter systems within BRF
- *serotonin*
- *acetylcholine*
- *dopamine*
- *noradrenaline*



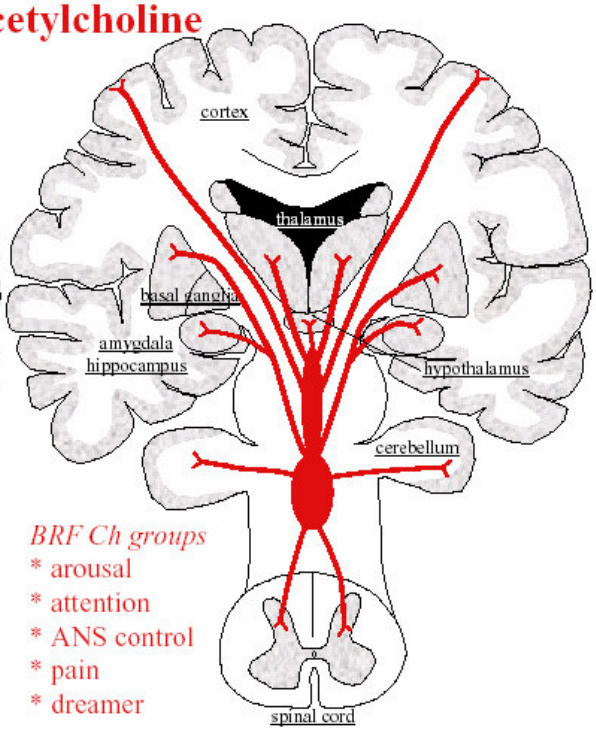
Neurotransmitter Systems of BRF

Serotonin



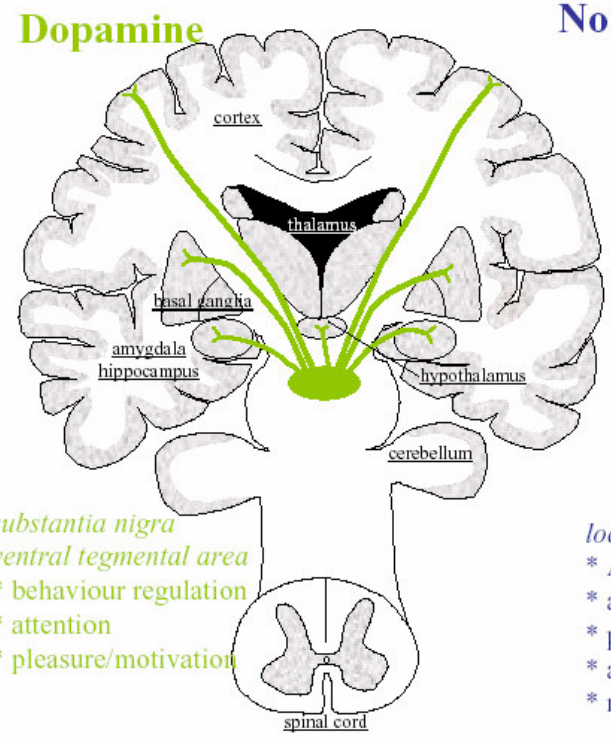
raphe nuclei
* behaviour
* aggression
* depression
* pain
* autoregulation

Acetylcholine



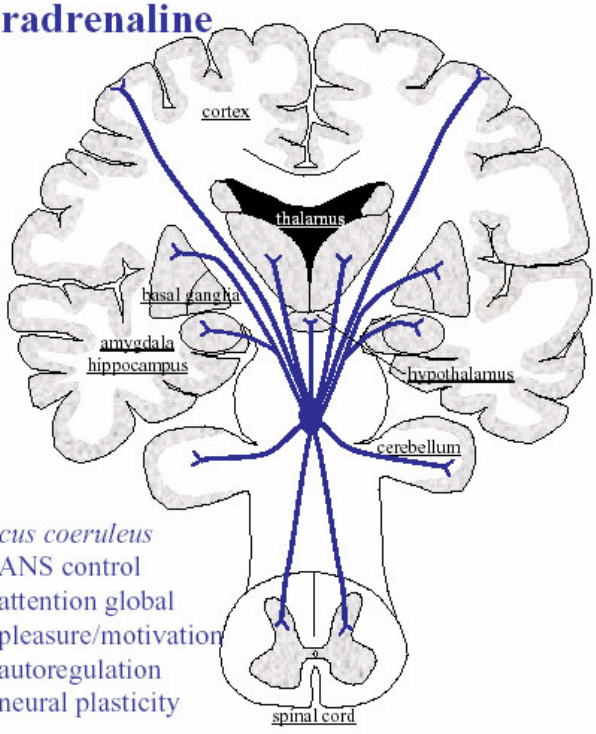
BRF Ch groups
* arousal
* attention
* ANS control
* pain
* dreamer

Dopamine



substantia nigra
ventral tegmental area
* behaviour regulation
* attention
* pleasure/motivation

Noradrenaline



locus coeruleus
* ANS control
* attention global
* pleasure/motivation
* autoregulation
* neural plasticity

MECHANISM OF PATHOLOGICAL CHANGES AFTER STROKE