By Adam Hollingworth

CNS Physiology

CSF Physiology 2

Functions CSF....3

CSF vs Plasma....3

ICP & It's Control 4

Pressure Volume Relationship....4

Determinants of Intracranial Volume....4

Cerebral Perfusion Pressure....5

Compensatory Mechanisms for ↑ed ICP....5

Intraocular Pressure 7

Factors Effecting IOP....7

Hypothalamus 8

1.Temp Regulation....8

2. Appetitive Behaviour....8

3.Control of Body Rhythms....9

4.Defensive Reactions....9

5. Control of Ant Pituitary Hormones....9

6. Production of Post Pituitary hormones....9

Physiology of Sleep 10

Electroencephalography (EEG) 12

Anaesthesia & EEG....12

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CSF Physiology

- CSF = fluid which bathes brain & spinal cord
- = transcellular fluid with composition identical to brain ECF
- produced by
  - choroid plexus 67%
  - ependyma of walls of ventricles & Pia mater (<33%)
- total volume ~150mls
- contained in ventricles & subarachnoid space
- daily production:
  - 500-600mls/day ie 24ml/hr
    - ↳ ∴ turnover x3-4/day
  - independent of ICP
    - ↳ (whereas absorption is proportional to ICP)
- CSF production:
  - First stage:
    - Plasma passively filtered across choroidal capillary endothelium
  - Second stage:
    - Active secretion of
      - water via aquaporins
      - ions – through apical membranes
- absorbed by (~500mls/day)
  - arachnoid villi 90%
  - directly into cerebral venules
- if ↑ICP arachnoid villi v important
  - ↳if ↑↑↑ICP ⇒ aquaporin channels in choroid plexus & other microvessels
- CSF ⇒ venous blood = bulk flow
  - ↳unidirectional
- CSF Absorption ∝ ICP:
  - Pressure 112mmH20 = pressure, filtration & absorption same
  - <68mmH20 absorption stops

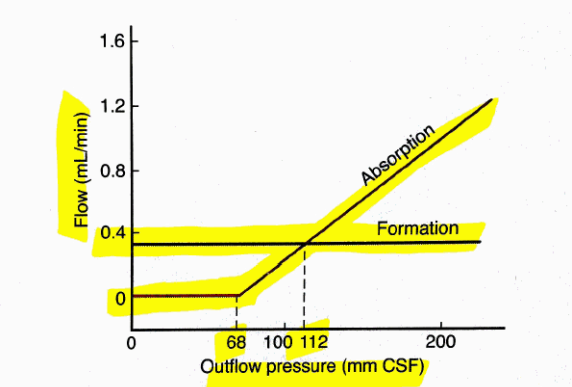


FIGURE 34–3 **CSF formation and absorption in humans at various CSF pressures.** Note that at 112 mm CSF, formation and absorption are equal, and at 68 mm CSF, absorption is zero. (Modified and reproduced with permission from Cutler RWP, et al: Formation and absorption of cerebrospinal fluid in man. Brain 1968;91:707.)

- CSF flows through aqueduct ⇒ foramens of Magendie & Luschka ⇒ subarachnoid space of brain & spinal cord

- Types of hydrocephalus:
  - Communicating hydrocephalus = ↓capacity reabsorption
  - Non communicating = blockage of vent system

Functions CSF

- protective - (also provided by arachnoid trabeculae)
  - dura attached to bone firmly
  - no subdural space – arachnoid & dura held together by thin fluid & surface tension
  - water bath effect ie like a cushion
  - 1400g brain effective weight of 50g
    - ↳ Why headache post LP – removal of CSF water bath ⇒ tension on nerve & vessels
- buffering rise in ICP ⟹ translocation of CSF into extracranial subarachnoid space
- return of interstitial protein to circulation - protein is absorbed with CSF across arachnoid villi
  - ↳ no lymphatics in brain
- nutritional

CSF vs Plasma

- PCO2 higher 50mmHg ⟹ CSF pH 7.33
- protein content v low (0.2g/l) ⟹ low acid base buffering capacity
- Lower glucose (but presence is handy for anaesthetists → diagnosis of unintentional dural puncture, -use urine “dipstix” to distinguish from eg Saline)
- electrolytes:
  - Urea and creatinine +/- same,
  - uric acid 1.5 vs 5 in plasma.
  - [Cl] is higher (124) +
  - [K] is lower (2,9)
  - [Mg] = higher (promotes neural stability)
  - Na and osmolality = same
  - Ca 2,5 vs 5 meq/L
- very low cholesterol content
- HCO_3 25.1 mmol/l vs 24.8 in plasma

∴ CSF content lower than plasma:

- Ca (most)
- K
- cholesterol
- pH
- protein
- glucose

CSF content higher than plasma:

- Pco2
- Cl
- HCO3
- Mg

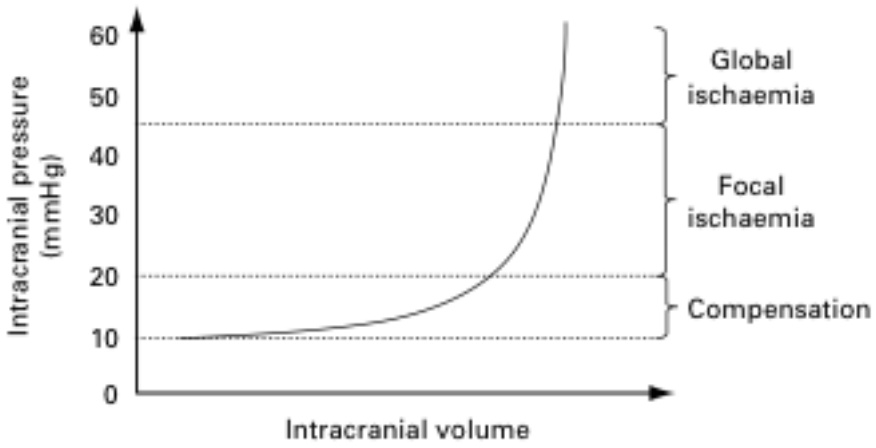
BUT osmolality same

ICP & It's Control

- normal ICP = 10-15mmHg
- threshold for mechanical brain injury = 20-30mmHg

Pressure Volume Relationship

- Monro-Kelly doctrine =
  - brain enclosed in a bony rigid skull
  - total volume of intracranial contents is fixed
  - any attempts to ↑volume of IC contents ⟹ rapid ↑pressure



- above curve = elastance curve
  ↳ because pressure / volume (ie inverse of compliance = V/P
  - brain tissue & fluid in the cranium are incompressible ∴ volume of blood, CSF & brain in the cranium must be relatively constant

Determinants of Intracranial Volume

- Cavity contains:
  - 1400g brain (1300 in female) (85%)
    - cushioned by CSF so effective weight = 50g
  - 75ml blood (5-10%)
    - CBF = 55ml/100g/min which = ~750ml/min ie ~15%CO
    - blood volume ↑ed with:
      - O_2/CO_2 levels:
        - PaO_2 = little ↑ until <50mmHg
        - $PaCo_2$ = double or half proportionally with $PaCo_2$
      - venous outflow obstruction eg ETT tie
      - valsalva
      - pain
      - vasoDilators
      - seizures
  - 75ml CSF in head (5-10%) :
    ↳ (75mls in spine = 150ml in total)
    - CSF volume ↑ed with:
      - outflow obstruction eg obstructive hydrocephalus
      - impaired uptake with arachnoid villi eg communicating hydrocephalus
      ↳ NB production fixed, reabsorption ↑es lineraly as ICP >10mmHg

Cerebral Perfusion Pressure

CBF = CPP/CVR

CPP = MAP - (higher of ICP or CVP)

- CPP <50 or >150mmHg ⟹ loss of cerebral autoregulation ⟹ flow is pressure passive
  ↳ same as uterus
- EEG effects @37deg C:
  - CPP <50mmHg ⟹ slowing EEG
  - 25-40 ⟹ flat EEG
  - <20mmHg ⟹ cell death if prolonged
    ↳ = <25ml/100g/min

- in head injured pt ie assumed ICP 20mmHg (no monitor):
  - should keep CPP >70mmHg
  - ie MAP >90mmHg

Compensatory Mechanisms for ↑ed ICP

- 5 mechanisms:
  - CSF translocation
  - ↑CSF absorption
  - ↓ed interstitial H2O
  - ↑MAP
  - unconsciousness ⟹ ↓CMRO2
- CSF translocation ie CSF ⟹ lumbar spinal sac
- ↑ed CSF absorption:
  - via arachnoid villi + venules
  - linear ↑ when ICP >10mmHg
- ↓ed interstsial H20 (minor)

↳ these 3 mechanisms quickly exhausted ⟹ rapid rise in ICP with any ↑ in intracranial volume

- Cushing reflex:
  - ↑MAP with ↓HR and ↑RR
  - MOA:
    - with falling CPP ⟹ low flow ⟹ cerebral ischaemia
    - stg 1: activation of SNS system ⟹ ↑ SVR & ↑HR ⟹ ↑MAP ⟹ restoration of CPP
    - stg 2: baroreceptors in arotic arch detect ↑MAP ⟹ ↑para symp output via vagus ⟹ bradycardia
      - MAP is maintained in order to defend CPP but HR slows
    - stg 3: ischaemia to brain stem ⟹ changes in RR with irreg pattern
- Unconciousness - with ↓CMRO2
  ↳ other ways to ↓CMRO2 = barbituates & cooling

Volatiles Effect on Cerebral Vasculature

- volatiles cause
  - direct cerebral vasoD:
    - N20 = most
    - isoflurane & sevoflurane the least
  - ↓ed MAP

↳ ∴ CPP may be <70mmHg ⟹ ↓CBF

- CMRO2 as effected by volatiles:
  - isoflurane - most
  - halothane - least

(thiopentone ⟹ ↓CMRO2 ++ ∴ neuroprotective)

- as dose anaesthetic agents ↑: autoregulation becomes ↑ingly pressure passive
  ↳ because cerebral vessels become max dilated
- also see an additive effect of CO_2 with volatiles in producing cerebral vasoD:
  ↳ ie slope of response curve ↑ed

∴ hypercarbia & deep volatile anaesthetic = bad!

Intraocular Pressure

- content of eye:
  - aqueous humour (behind cornea)
  - vitreous humour (behind lens & in front of retina)
- norm IOP 10-20mmHg - but see small diurnal variation with ↑night
- IOP helps to maintain shape of eye
- IOP dependant on:
  - aqueous volume - balance production & absorption
  - choroidal blood volume - non compliant sclera ⟹ ↑blood volume ⟹ rapid ↑IOP
  - external pressure eg blinking
- aqueous humour:
  - total volume ~0.3ml
  - humour made in cilary body of post chamber:
    - 2/3 = active - carbonic anhydrase dependant reaction (∴ inhibited by acetazolimide)
    - 1/3 = passive filtration from ant surface of iris
  - absorbed via trabecula meshwork ⟹ spaces of Fontana & venous canal of Schlemm trabecular meshwork ⟹ calan
- Canal of Schlemm
  - located between iris & cornea at angle of ant chamber
  - obstruction of this ⟹ ↑IOP ⟹ damage to retinal nerves
    ↳ ie glaucoma

Factors Effecting IOP

- Physiological:
  - aqueous humour:
    - ↓drainage
      - ↑venous pressure eg cough, strain
      - mydriasis - closes angle between iris & trabecula meshwork
    - ↑drainage:
      - ↓ITP
      - head tilt up
      - miosis
  - choroidal blood volume:
    - ↑blood
      - ↑$PaCO_2$ via vasoD
      - large ↑MAP
      - large ↓PaO_2 ⟹ vasoD
    - ↓blood volume:
      - ↓$PaCO_2$
  - Extraoccular pressure:
    - blinking - ↑IOP by 10-20mmHg
    - pressure - eg weight after eye block
- Pharmacological control:
  - Mannitol - rapid ↓aqueous humour production
  - CA inhibitor (amiloride) - ↓rate of production
  - ßBlocker - ↓production & miosis
  - muscarinic agonists - miosis ∴ ↑drainage

- prostaglandin analogue ⟹ ↑drainage

Hypothalamus

- main functions:
  - temp regulation
  - appetitive behaviour:
    - water balance
    - behaviour (sexual)
    - appetite
  - defensive reactions
  - Control Body Rhythms
  - neuroendocrine control ant pit hormones
  - production of post pituitary hormones

1.Temp Regulation

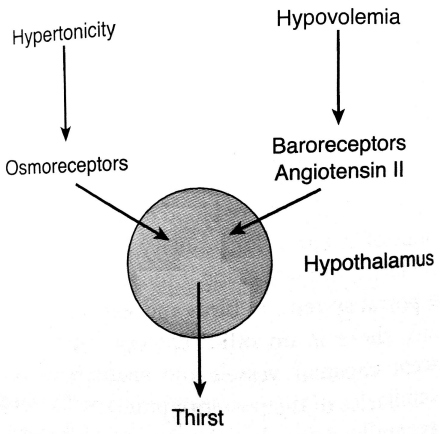
- receives afferents from:
  - skin - cold x10 > warm receptors
  - spinal cord
  - abdo viscera
  - around deep veins
  - hypothalmic preoptic area
- post HT generates signals needed for heat production ⟹ phagocytic cells produce IL-1
- IL1 = endogenous pyrogen ⟹ stim anterior HT to produce PGE2 ⟹
  - ↑ thermostat set point to heat conservation (vasoC)
  - ↑heat production (shivering)

  ↳ allows temp of body to reach new set point

2. Appetitive Behaviour

Water Balance

- osmoreceptors in ant HT (outside bbb esp organum vasculosum of lamina terminalis) sense change in osmolality
- ⟹ integrates input
- ⟹ effectors ie thirst & ADH release
- drinking regulated by
  - osmoreceptors
  - ↓ECF volume
  - psychological factors



- control of thirst & ADH release = most important effector responses:
  - osmoreceptors in anterior HT
    - ⟹ thirst initiated in HT
  - volume receptors
    - venous system
    - high pressure arterial baroreceptors
      ↳ have neural input to HT ie can ↑ or ↓ thirst or ADH release
    - renin-A-A axis also involved in volume control:
      - hypovolaemia ⟹ ↑renin secretion ⟹ ↑AT-2 input to SFO & organum vasculosum of lamina terminalis ⟹ ↑thirst & ADH release
- ADH:
  - produced in supraoptic & paraventricular nuclei in HT
  - travels down axons for storage in post pituitary

Behaviour/Emotions

- afferents from limbic areas (emotion & sexual activity) ⟹ integrated in lat & post HT
- parasympathetic NS inputs ⟹ ant HT
- symp NS ⟹ post HT

Appetite

- lateral HT = hunger & appetite
- antero-medial nucleus:
  - glucostat cells sensitive to rate of glucose utilisation
  - leptin receptors

  ↳ balance calory intake & energy expenditure

3.Control of Body Rhythms

- retina via retino-hypothalamic fibres

4.Defensive Reactions

- sense organs & neocortex
- unknown input paths
- diffuse integration throughout HT & limbic system

5. Control of Ant Pituitary Hormones

- see endocrine notes

6. Production of Post Pituitary hormones

- see endocrine notes

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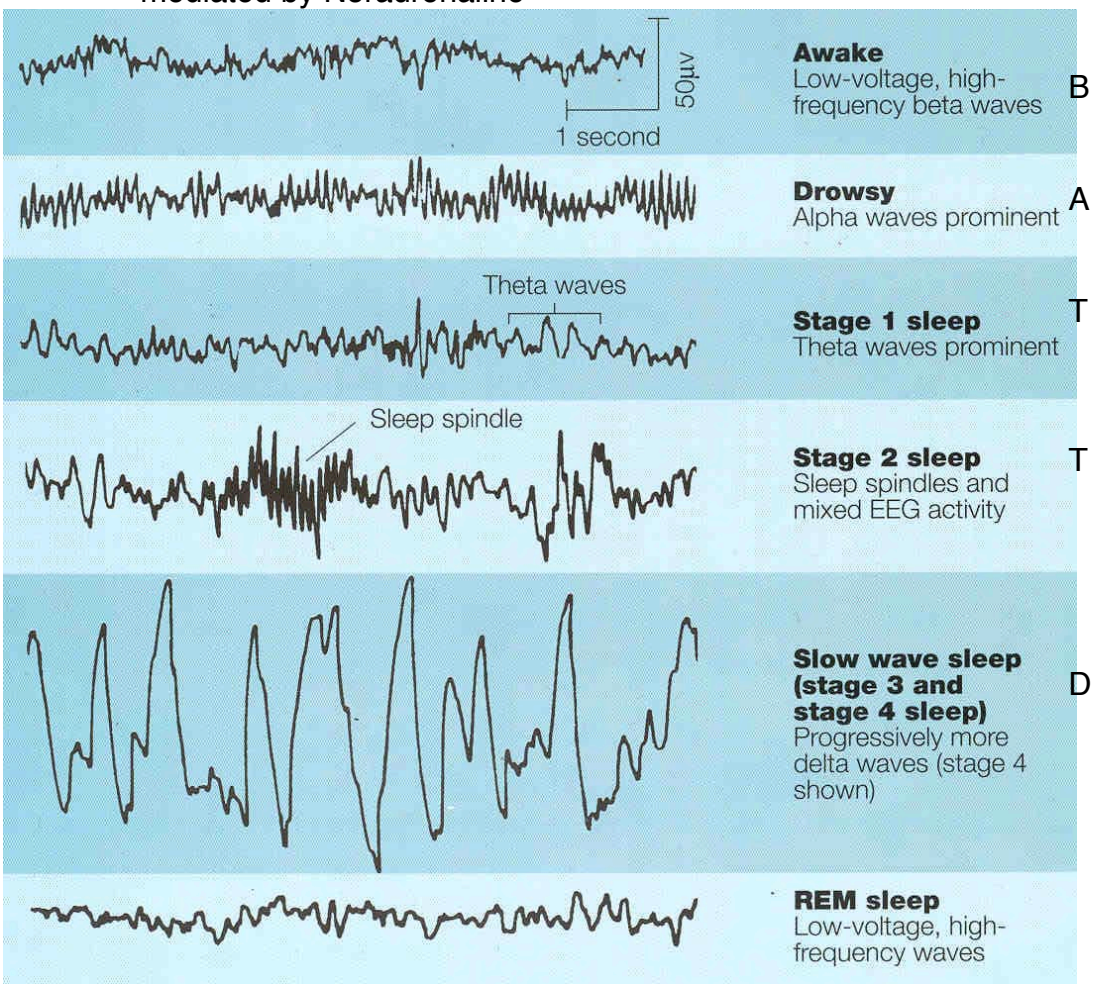
Physiology of Sleep

- sleep = naturally occurring state of reversible unconsciousness. Response to external stimuli is decreased but still possible.
- can categorise sleep based on EEG patterns:
  - awake = beta waves
  - drowsy = alpha waves
  - non REM sleep : has 4 stages (B.A.The.D)
    - 1: theta waves - as falling asleep. Low amplitude, high frequency waves
    - 2: sleep spindles & K complexes = alpha like bursts of activity 10-14Hz
    - 3 & 4: delta waves with:
      - ↑ing coherence,
      - slowing frequency,
      - amplitude ↑s
  - REM sleep:
    - rapid, irregular, low amplitude waves - very similar to awake EEG
    - see:
      - dreaming, rapid eye movements
      - ↑HR, ↑RR - irregular pattern
      - skeletal mm ↓tone
      - penile erection
      - ↑glucocorticoid production

    ↳ mediated by Noradrenaline



B waves

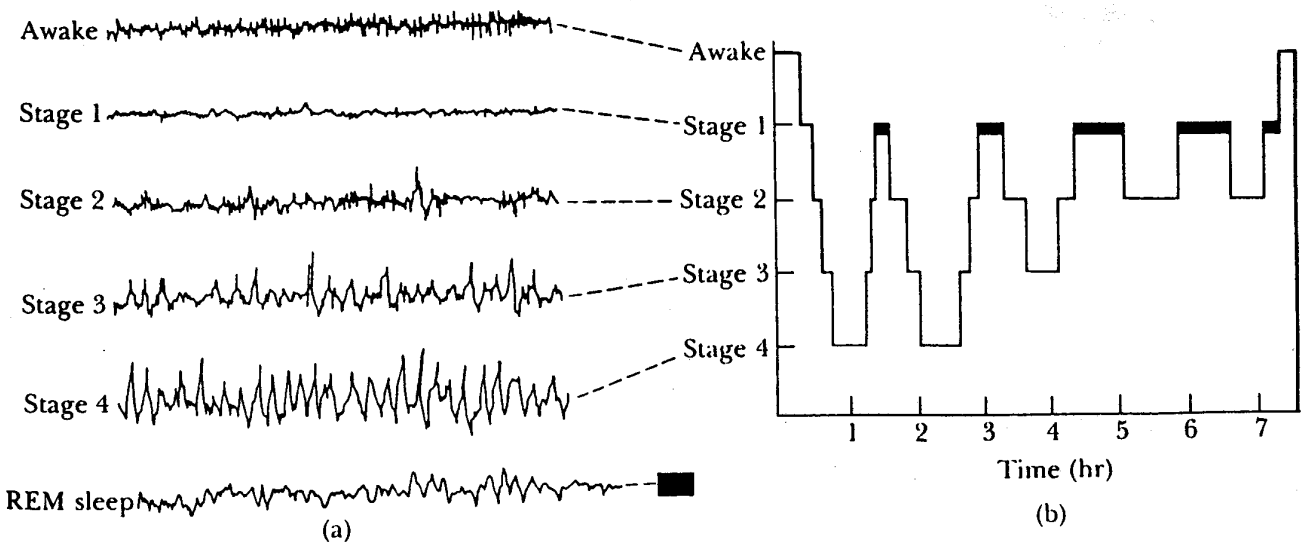
A waves

T waves

T with spindle & K complex

D waves

- typical nights sleep:



  - rapid pass through stages 1&2 ⟹ ~60-90 min in stage 3+4 sleep
  - period of REM sleep follow lasting ~60-90min
  - cycle repeats ⟹ ~5 episodes of REM/night
- amount of slow wave sleep ↓s with age
- age makes a difference:
  - neonates ~45-65% REM sleep
  - >50yrs ~15% REM sleep

- metabolic rate ↓10% in sleep
- O_2 consumption highest in REM & lowest in stage 3&4
- resp changes:
  - PCO_2 vent response ↓↓↓REM sleep (mostly unchanged in stage 3&4)
    ↳ PO_2 response unchanged in all stages
  - Vt :
    - REM = markedly ↑↑ed
    - non REM = mod ↓ed
  - RR slight ↑ed. ∴ PCO_2 ↓ed by 3mmHg

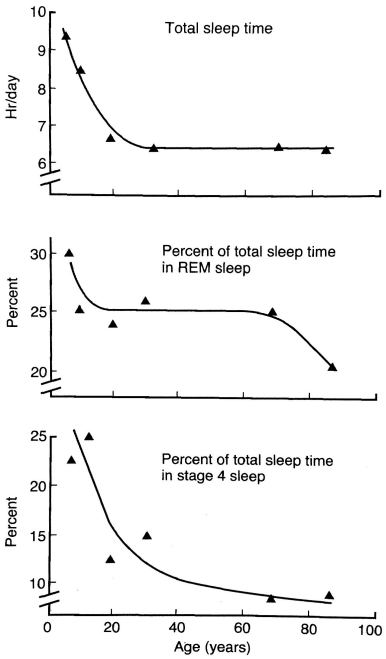


FIGURE 15–9 Changes in human sleep pattern with age. Each plot shows data points for the ages of 6, 10, 21, 30, 69, and 84 years. (Data from Kandel ER, Schwartz JH, Jessel TM [editors]: *Principles of Neural Science*, 4th ed. McGraw-Hill, 2000.)

Electroencephalography (EEG)

- = surface recording of electrical activity of brain
  - ↳ only reads superficial dendrites which lie perpendicular to surface of cortex
- small voltage compared to ECG (50uV vs 2000uV)
- signals from various combinations of 20-22 scalp electrodes presented as 16 continuous traces
  - ↳ = raw or unprocessed EEG
- shape, distribution, incidence & symmetry of waves are analysed
- concealed abnormalities may be revealed by ↓$PaCO_2$ ie hyperventilation
- rhythms:
  - alpha =
    - normal awake
    - 8-13Hz waves
    - prominent at parieto-occiptial area at rest with closed eyes
  - Beta =
    - normal awake
    - 13-30Hz
    - prominent over frontal area
  - delta =
    - abnormal awake (may see in kids, or when asleep)
    - <4Hz
  - theta:
    - sometimes abnormal awake
    - 4-8Hz
- with ↑age infantile beta activity slowly replaced by adult alpha activity

Anaesthesia & EEG

- B.A.The.D ie beta ⟹ alpha ⟹ theta ⟹ delta
- general trend is for ↓frequency & ↑amplitude
- @ deeper levels of anaesthesia:
  - slow rhythms ⟹ periods of little/no activity separated by bursts of activity (burst suppression)
- different anaesthesia agents result in diff EEG patterns
- processed EEG's used in depth of anaesthesia monitoring eg BIS & entropy monitoring - see monitoring notes

- eg seizure pattern: = spike & dome pattern