CNS Physiology

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By Adam Hollingworth
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
    - independent of ICP
  - turnover x3-4/day
- 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 112mmH2O = pressure, filtration & absorption same
  - <68mmH2O absorption stops

CSF flows through aqueduct ⇒ foramen 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
- HCO3 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

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:
      - O2/CO2 levels:
        - PaO2 = little ↑ until <50mmHg
        - PaCO2 = double or half proportionally with PaCO2
      - 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 linearly 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 interstisial 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 aortic 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

- Unconcosnousness - 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 \implies \downarrow \text{CBF}

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

(thiopentone \implies \downarrow \text{CMRO2} ++ \implies \text{neuroprotective})

- as dose anaesthetic agents ↑: autoregulation becomes ↑ingly pressure passive
  - because cerebral vessels become max dilated
- also see an additive effect of CO2 with volatiles in producing cerebral vasoD:
  - ie slope of response curve ↑ed
- \therefore \text{hypercarbia} & \text{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
      • ↑PaCO2 via vasoD
      • large ↑MAP
      • large ↓PaO2 ⇒ vasoD
    - ↓blood volume:
      • ↓PaCO2
  - Extraocular 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
  - βBlocker - ↓production & miosis
  - muscarinic agonists - miosis ↓⇒ ↑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
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
• typical nights sleep:

- rapid pass through stages 1&2 ⇒ ~60-90 min in stage 3+4 sleep
- period of REM sleep follow lasting ~60-90 min
- 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
- O2 consumption highest in REM & lowest in stage 3&4
- resp changes:
  - PCO2 vent response ↓↓↓REM sleep (mostly unchanged in stage 3&4)
    → PO2 response unchanged in all stages
  - Vt:
    - REM = markedly ↑↑ed
    - non REM = mod ↓ed
  - RR slight ↑ed. ∴ PCO2 ↓ed by 3mmHg
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 ↓PaCO2 ie hyperventilation
- rhythms:
  - alpha =
    - normal awake
    - 8-13Hz waves
    - prominent at parieto-occipital 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