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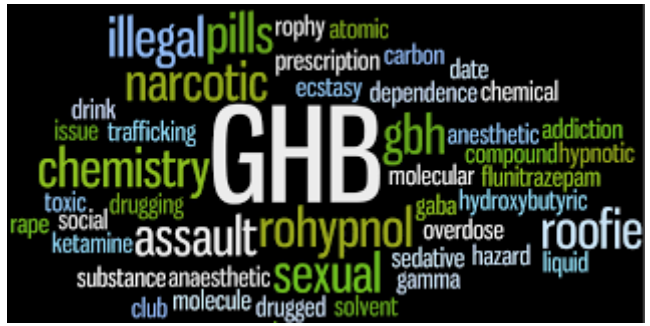
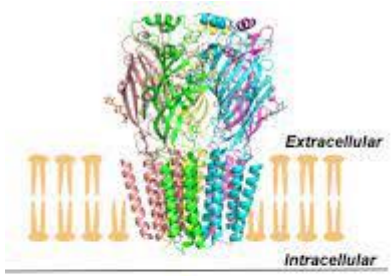
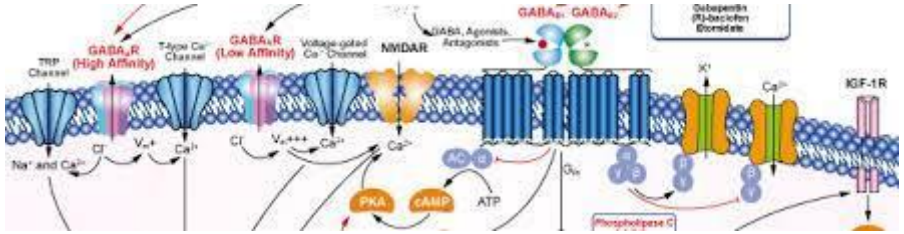


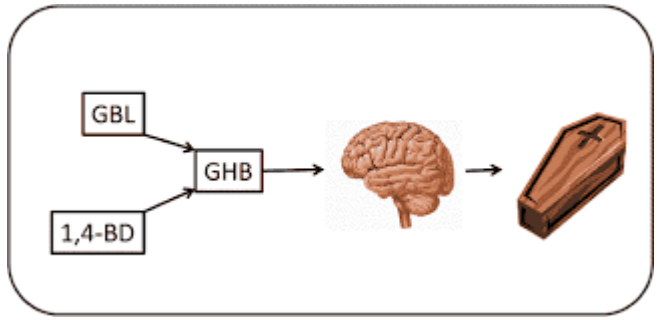


GHB withdrawal

Dr D M Lloyd-Jones



GHB intoxication



- Not under discussion today
- Note- the management of GHB intoxication may impact on the withdrawal
- Rapid onset of anxiolysis, euphoria, sedation
- Frequent LOC common! (daily)- steep dose-response curve
  - GHB coma often trivialised by users

Gammahydroxybutyrate (GHB)

- euphoric, stimulant, sedative, sexual effects
    - clear, odourless, salty liquid “stale water”, “burnt plastic”
    - powder, capsules, tablets

- Dietary supplements- used in bodybuilding (purported anabolic effects), insomnia, anxiety, alcohol dependence

- Analogues are: GBL (shorter onset of action, greater potency, longer duration of effect); 1,4 butanediol

- Nightclubs, dance parties, MSM, bodybuilders, chemsex

- Often associated with use of stimulants and alcohol

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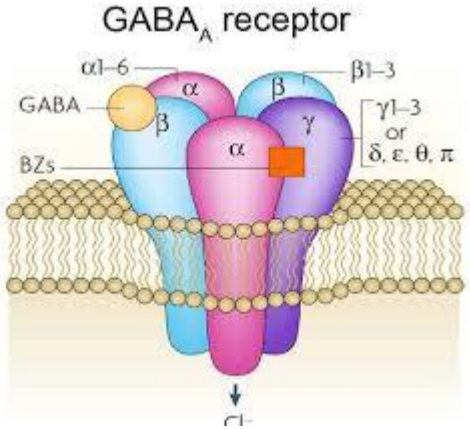
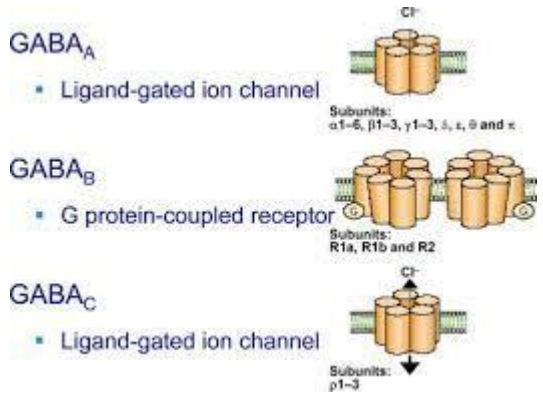
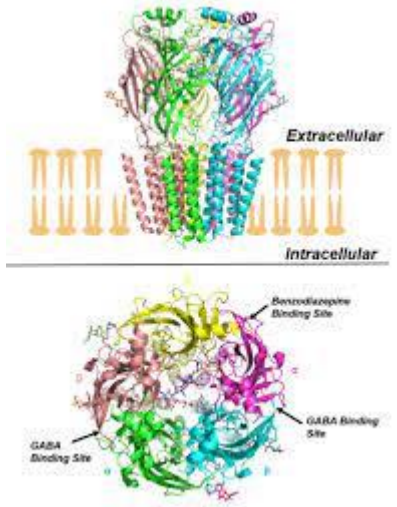
pharmacology

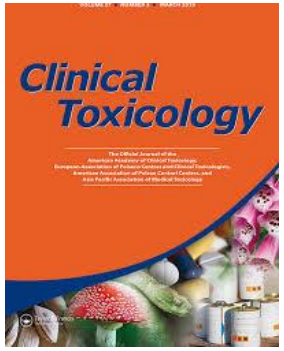
- GHB-specific receptors and GABA-B receptors (? Also GABA-A receptors)
    - neuromodulatory effects on GABA, dopa, glutamate, serotonin, NA, cholinergic systems and neurosteroidogenesis and oxytocin release
- Chronic use – downregulation of inhibitory GABA and GHB receptors. Thus abrupt cessation leads to unopposed excitatory neurotransmission (similar to ETOH withdrawal)

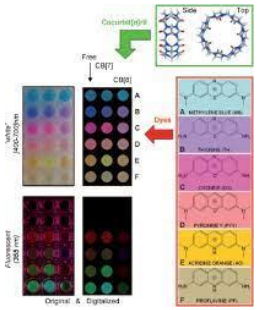






identification





- Onset within 15-30 mins
- Sedation usually lasts 3-6 hrs
- Unconsciousness/blackouts can last up to 24 hrs post ingestion

- 95% met in liver
- T1/2 30-60 mins so 50% eliminated within one hour (metabolism increased when mixed with alcohol)`

- Saliva- detection range 10 mins-6hrs
- Urine- detection range up to 2-12 hrs (test must be performed rapidly to be valid)
- Blood- detection up to 72hrs post ingestion (peak at 30 mins)

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Dependence is hard to treat

- GHB use – high rates of ED attendance
- Highest treatment intensity
- Highest chance of readmission

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Withdrawal

- Similar to ETOH withdrawal but more rapid and abrupt onset and more prominent neuropsychiatric symptoms
  - Tremor, diaphoresis, anxiety, agitation, confusion, **delirium**, psychosis
  - Severe refractory withdrawal symptoms can occur and may reflect delayed/inadequate treatment

- Severe withdrawal can occur with frequent dosing over as short a period as 7-10 days
  - Mean daily dose of 56g (10-312g)
  - Symptoms can occur after 30 mins of last dose
  - If >6 hrs post last dose may experience severe withdrawal

Delirium

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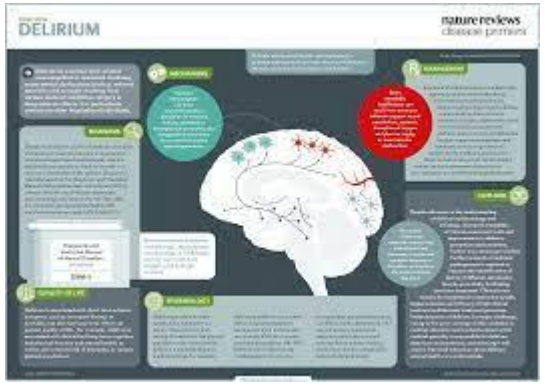
- Common
- Can be severe, prolonged and refractory to bzds



Differentials

- Other sedative/alcohol withdrawals
- Acute GHB intoxication
- Intoxication with sympathomimetics (ephedrine, pseudoephedrine)
- Anticholinergic syndrome
- Hypoglycaemia
- Seizures
- Serotonin syndrome
- Thyroid storm
- NMS
- HI
- CNS infection/inflammation (encephalitis, meningitis)
- Functional psychosis

Complications

- Severe withdrawal can last 2-15 days in ICU, complications may require longer stays (up to 32 days)
- Profound insomnia
- May be initial improvement followed by rapid deterioration
- Hallucinations
- Delirium
- Seizures (in 7%)
- Rhabdomyolysis (7%), AKI, coma, death
    - Autonomic disturbances usually mild cf. ETOH withdrawal.
    - Tremor and diaphoresis often present early
- If co-used with stimulants- agitation, tachycardia more common

Investigations

- GHB can be detected on GCMS- may take 7-10 days
    - GHB in blood for 4-6 (can be longer)hrs
    - GHB in urine if < 6-12 hrs post ingestion
- Investigations only if needed to target diff diagnoses/complications
    - U&Es, BSL etc
    - CK
    - FBC
    - Paracetamol levels
    - ECG
    - Preg test
    - “Tox screen”

Management

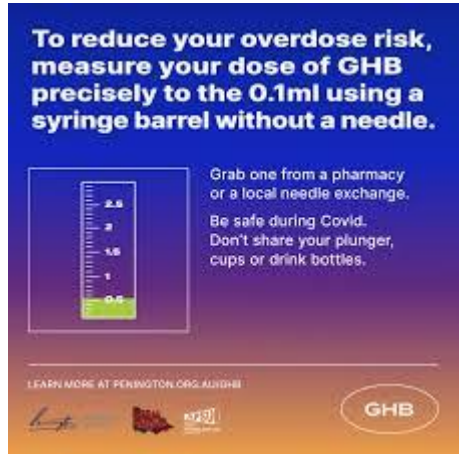
- No RCTs. Retrospective case series, nonrandomised prospective studies
- (inpatient) Pharmaceutical GHB titration and taper

- BZDs + baclofen

- Efforts to control agitation and delirium may require intubation and ventilation

In-patient vs Out-patient management

- Admit if:
  - >30ml or g/day for > 2 weeks
  - Using > 3x/day
  - Previous severe withdrawal symptoms
  - Currently confused/hallucinating
  - Polysubstance use and withdrawal likely
  - Significant medical/psychiatric co-morbidity



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- >30g (ml), >15g GBL of GHB associated with more severe withdrawal
- Dosing >3x/day associated with more severe withdrawal
- Early onset of symptoms associated with more severe symptoms

- Rapid and aggressive symptom suppression- diazepam, can be iv
  - Monitor pulse oximetry or preferable end-tidal CO2
- Barbiturates- phenobarbital, pentobarbital
- Propofol
- Dexmedetomidine

Severe withdrawal with delirium

- HDU/ICU
- High dose bzds
- Intubation and ventilation
- Monitor for hyperthermia, rhabdomyolysis (CK)

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pharmaceuticals

- Bzds
    - Diazepam iv 10mg every 5-10 mins
    - Note iv diazepam has a rapid onset of action (5 mins) but a high volume of distribution (adipose tissue) – may require repeat doses until total body loading
    - iv lorazepam has low lipid solubility and short half-life so less appropriate
    - oral sufficient if less severe (<32g GHB/day- give 20-80mg diazepam)
    - Loading doses do not reduce likelihood of withdrawal delirium but reduce severity of delirium
- If 100mg of iv diazepam over 60 mins fails to control symptoms the addition of barbiturates/propofol

- Doses of bzds (+ barbiturates) may then be tapered over SEVERAL weeks

Severe GHB withdrawal delirium managed with dexmedetomidine

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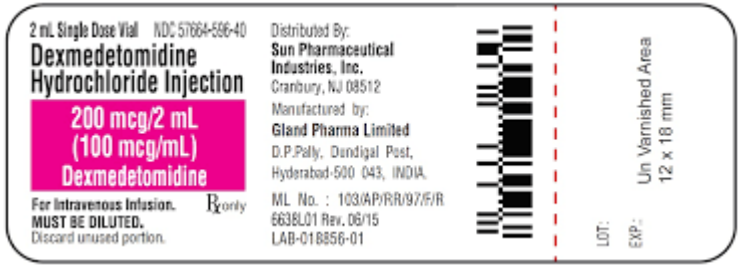
- Case report
- 23 yof
- Severe agitation after admission to private "detox" facility
- Had used MA and GHB earlier that day and had presented well on admission
- GHB and GBL dependence > 2 yrs
    - Up to 36ml GHB/GBL/day
    - 3 points MA/day
    - 25mg diazepam/day
- Depression→Venlafaxine
- ADD- previously treated with methylphenidate
- Agitated and responding to hallucinations, diaphoretic, tachycardia, tremulous
- Inattentive, paranoia



The MENDS2 Trial:
Dexmedetomidine vs Propofol for Sedation

REBEL CRIT

Management

- Physical restraints
- Delirium work-up
- 65mg diazepam, 50mg quetiapine, 10mg olanzapine in first 24 hrs- with little benefit
- Transfer to ICU
    - where dexmedetomidine was commenced and titrated to effect and SE (bradycardia, hypotension)
    - Diazepam 30-55mg/day
- Remained agitated by Day 5, 1:1 nursing care
- Most symptoms had subsided by Day 14- discharged back to private facility

references

- GHB withdrawal management. Government of SA. SA Health
- Severe GHB withdrawal delirium managed with dexmedetomidine
- GHB withdrawal and dependence- UpToDate
- Management and Detoxification for Gamma-Hydroxy-Butyrate (GHB) and Gamma-Butaryl-Lactone (GBL) Policy. Camden and Islington NHS Trust. Aug 2019

- If in doubt call DACAS 1800 812 804

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Do you have
any
Questions?