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NEUROLOGICAL SEQUELAE OF SUBSTANCE MISUSE

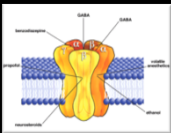
Learning Objectives

By the end of the sessions, students should be able to:

- Be aware of the principles of how to make an assessment of drug and alcohol use in a variety of clinical settings.
- Be able to describe appropriate assessment, **examination** (physical, **mental state** and **cognitive**) and clinical investigation for the consequences of substance misuse.
- Describe and explain the links between substance misuse (primarily alcohol) and the following neurological conditions.
 - Seizures (including withdrawal seizures and impaired epileptic control)
 - Wernicke / Korsakoff Syndrome
 - Chronic cognitive impairment
 - Paraesthesia
 - Stroke
- Be aware of specific interventions a Foundation Doctor may instigate in these circumstances

Alcohol Withdrawal

- EtOH
 - increases (inhibitory) GABA-R activity
 - antagonises (excitatory) NMDA-R
- Withdrawal -> **↑excitatory activity**



GABA-R

Alcohol Withdrawal

- Spectrum
 - Minor (>50%)
 - Major
 - Seizures
 - Delirium Tremens (<5%)
- Risk Factors:
 - ?
 - ?

| Intoxication | Withdrawal |
|---------------|---------------|
| ↑ GABA | ↓ GABA |
| ↑ Glycine | ↓ Glycine |
| ↑ Dopamine | ↓ Dopamine |
| ↓ Epinephrine | ↑ Epinephrine |
| ↓ Serotonin | ↑ Serotonin |

Alcohol Withdrawal

- Spectrum
 - Minor (>50%)
 - Major
 - Seizures
 - Delirium Tremens (<5%)
- Risk Factors:
 - Heavy EtOH intake
 - Past history of seizures and/or DT (kindling)

| Intoxication | Withdrawal |
|---------------|---------------|
| ↑ GABA | ↓ GABA |
| ↑ Glycine | ↓ Glycine |
| ↑ Dopamine | ↓ Dopamine |
| ↓ Epinephrine | ↑ Epinephrine |
| ↓ Serotonin | ↑ Serotonin |


Alcohol Withdrawal

- Spectrum
 - Minor (6-24hrs)
 - Tremor
 - Anxiety & insomnia
 - N&V

| Intoxication | Withdrawal |
|---------------|---------------|
| ↑ GABA | ↓ GABA |
| ↑ Glycine | ↓ Glycine |
| ↑ Dopamine | ↓ Dopamine |
| ↓ Epinephrine | ↑ Epinephrine |
| ↓ Serotonin | ↑ Serotonin |

Alcohol Withdrawal

- Spectrum
 - Minor (6-24hrs)
 - Major (10-72hrs)
 - Hallucinations (visual/auditory/tactile)
 - Tremor+
 - Sweating, hypertension

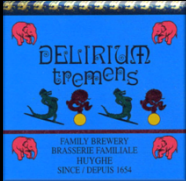


Alcohol Withdrawal

- Spectrum
 - Minor (6-24hrs)
 - Major (10-72hrs)
 - Seizures (6-48hrs)
 - Multiple brief generalised seizures (usu over 6hrs)
 - 3% develop status epilepticus
 - >1/3 develop delirium tremens

Alcohol Withdrawal


- Spectrum
 - Minor (6-24hrs)
 - Major (10-72hrs)
 - Seizures (6-48hrs)
 - Delirium tremens (3-10 days)
 - A medical emergency: mortality 5-15% (arrhythmias, etc)
 - Agitation & delirium, intense fear
 - Autonomic hyperactivity (↑BP, HR, T, sweating)



Alcohol Withdrawal Rx

- Chlordiazepoxide reducing regime
daily U = qds dose (& prn)
- Also prophylaxis vs Wernicke's
- Seizures: i.v. Diazepam



| Dayly units or SADD score | 100U / 4 AD030 | 25U / SADD 25 | 20U / SADD 20 | 15U / SADD 15 |
|---------------------------|----------------|---------------|---------------|---------------|
| Monday | 30 mg QDS | 25 mg QDS | 20 mg QDS | 15 mg QDS |
| Tuesday | 25 mg QDS | 20 mg QDS | 15 mg QDS | 10 mg QDS |
| Wednesday | 20 mg QDS | 15 mg QDS | 10 mg QDS | 10 mg TDS |
| Thursday | 15 mg QDS | 10 mg QDS | 10 mg TDS | 5 mg TDS |
| Friday | 10 mg QDS | 10 mg TDS | 5 mg TDS | 5 mg BD |
| Saturday | 10 mg TDS | 5 mg TDS | 5 mg BD | 5 mg OD |
| Sunday | 5 mg TDS | 5 mg BD | 5 mg OD | |
| Monday | 5 mg BD | 5 mg OD | | |
| Tuesday | 5 mg OD | | | |



Wernicke/Korsakoff Syndrome

2 syndromes:



- Wernicke (acute/subacute)
 - Confusion
 - Ataxia
 - Nystagmus/Ophthalmoplegia
- Korsakoff (chronic)
 - Anterograde amnesia

Wernicke/Korsakoff Syndrome

2 syndromes:

- Wernicke (acute/subacute)
 - Confusion
 - Ataxia
 - Nystagmus/Ophthalmoplegia (same symps as Benzodiazepine OD)
- Korsakoff (chronic)
 - Anterograde amnesia

Wernicke/Korsakoff Syndrome

Cause: thiamine (B₁) deficiency (18 days of stores)

- EtOH reduces duodenal transport;
- CLD reduces activation and storage of thiamine
- Nutritional deficiency
- IATROGENIC** administration of glucose

Wernicke/Korsakoff Syndrome



- Result: impaired metabolism in specific brain regions
 - Ataxia
 - Nystagmus/Ophthalmoplegia
 - Amnesia

Wernicke/Korsakoff Syndrome

- On examination
 - Eye signs:
 - Motor signs:
 - Cognitive...

Wernicke/Korsakoff Syndrome

- On examination
 - Eye signs: diplopia, nystagmus, LR palsy
 - Motor signs: ataxia, broad based gait, past pointing, etc
 - Cognitive...



Cognitive Examination


- MMSE
 - Orientation in time (5) & place (5)
 - Registration of 3 objects (3)
 - Attention: serial 7's or D-L-R-O-W (5)
 - Recall of 3 objects (3)
 - Naming (2), reading (1), writing (1), repeating (1), understanding command (3)
 - Copying figure (1)

Cognitive Examination

- MMSE
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Cognitive Examination

- MMSE
- Episodic memory
 - What did you do today/how did you get here?
 - Recent news
 - Where were you on X date?
 - Significant personal events



A collage of images including newspaper clippings with the headline 'DIANA IS DEAD', a photo of a wedding ring, and other news snippets.

Wernicke/Korsakoff Syndrome

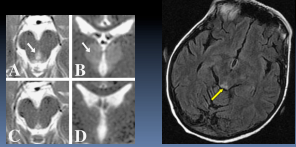
- On examination
 - Eye signs: diplopia, nystagmus, LR palsy
 - Motor signs: ataxia, broad based gait, ddk
 - Cognitive:
 - MSE: disorientation, poor attention/concentration, poor recall
 - Memory: recent news, autobiographical recall
 - Confabulation?

Wernicke/Korsakoff Syndrome

Confabulation

Wernicke/Korsakoff Syndrome

- Investigations
 - Exclude other causes of confusion
 - Metabolic
 - Infectious
 - Cerebral (incl vascular)
 - Diagnosis




Wernicke/Korsakoff Syndrome

- Treatment – A MEDICAL EMERGENCY
 - Thiamine i.v. Pabrinex I & II (bd for 3 days)
 - ?other electrolytes
 - B vitamins
 - DON'T GIVE GLUCOSE without THIAMINE
 - Treat withdrawal

But...

- Symptoms are unreliable
 - Only 10% pts have the triad
 - <30% have eye signs
- Alcoholics tend to be drunk (i.e. confused, ataxic)
- There is no simple blood test



Therefore...

- Treat any chronic alcoholic with >1 symptom (drunk or not)
- DON'T EVER GIVE GLUCOSE WITHOUT PABRINEX FIRST!

Alcoholic Cognitive Impairment

- NOT Wernicke-Korsakoff's
- Neurotoxicity in frontal cortex, CBM (esp with repeated withdrawal)
- Diagnosis:
 - Dementia (memory deficit plus one other function, prob executive)
 - Hx heavy drinking (but not for 2/12 prior to Dx)
- Prognosis stable +/- some recovery if abstinent

Cognitive Examination

- MMSE
 - Orientation in time (5) & place (5)
 - Registration of 3 objects (3)
 - Attention: serial 7's or D-L-R-O-W (5)
 - Recall of 3 objects (3)
 - Naming (2), reading (1), writing (1), repeating (1), understanding command (3)
 - Copying figure (1)

Cognitive Examination

- MMSE
- Frontal tests
 - Proverbs & Cognitive estimates
 - Go-NoGo
 - Fist-edge-palm (Luria)
 - Verbal fluency

Alcoholic Neuropathy

- Direct neurotoxicity of EtOH, +/- thiamine deficiency
- Symptoms:
 - Slowly progressive sensory & motor neuropathy
 - Numbness -> Parasthesia -> Pain (esp at night)
 - Glove and stocking distribution
 - Sensory ataxia



Alcoholic Neuropathy

- Differential diagnosis:
 - Diabetes
 - B12 deficiency
 - Pressure
- Diagnosis:
 - Alcohol history
 - Nerve conduction studies
- Treatment:
 - Stop EtOH
 - Vitamins



Stroke

- EtOH's benefits in low dose are reversed at higher dose
 - Hypertension
 - Trauma (usu SDH rather than CVA) –NB ↑ INR
 - Arrhythmias/Cardiomyopathy are pro-thrombotic
- Causes of CVA in lower age groups

For FY1 survival...

- Assess need for chlordiazepoxide RR
- Giving i.v. thiamine (Pabrinex I + II) to alcoholics at risk
- NOT giving i.v. glucose before thiamine
- 'Confusion in an alcoholic' work-up
 - Drunk? Detoxing? Wernicke's? Dementia?
 - Other causes (infection, metabolic, trauma, etc)
- Check alcoholic's feet
