BIOP211 – Pharmacology
Tutorial Session 11 Anticonvulsants, Alcohol, Drug Abuse

- Students research the effects of alcohol across body systems and investigate drug abuse, dependence and tolerance
- Students review anti-convulsants, drugs used in degenerative disease, affective disorders and schizophrenia

11.1 Discuss these pharmaceutical medications.

- Sedatives and anxiolytics
- Monoamine oxidase inhibitors (MAOI), selective serotonin reuptake inhibitors (SSRIs), tri-cyclic antidepressants (TCA) and the treatment of depression
- Lithium and the treatment of bipolar disorder and mania
- Anti-epileptic drugs
- Antipsychotics in the treatment of schizophrenia

Your answer should cover the following

- Examples and indications
- Mechanism of action
- Efficacy and limitations or cautions / contra-indications
- Adverse effects and drug interactions with nutrients and herbs

Mark your own answers using the Pharmacology text or online resources. Alternatively, peer review each other’s answers, allocating 10 marks per drug class

11.2 Case Study – Use your textbook. Discuss in forums or in class.

Drugs Affecting the CNS – Anti-psychotics

Peter was diagnosed with Schizophrenia at age 21 years. He has a history of recreational drug use as an adolescent.

1. Which recreational drugs can contribute to the onset of schizophrenia?
2. What symptoms/behaviour may Peter exhibit? What is the difference between positive and negative symptoms?

He was started on Chlorpromazine but exhibited some adverse effects

3. What adverse effects may he be experiencing as a result of this medication? What is the mechanism of action of this drug?

He was changed to Clozapine

4. What is the advantage of this drug over Chlorpromazine? What adverse effects may be experienced with this drug?
11.3 Anti-Convulsants, Drugs used in Degenerative Disease, Affective Disorders, and Drugs of Abuse - Use your textbook. Feedback is available in Review Quiz Session 11.

Multiple Choice Questions for Review

1. A patient tells you that their epileptic fits involve a feeling of confusion, a black out and a chewing type of facial movement. This is characteristic of which type of epilepsy?
   a) Transient ischaemic attack
   b) Partial complex
   c) Psychogenic
   d) Myoclonic

2. Which of the following types of epilepsy is a clinical emergency?
   a) Status epilepticus
   b) Tonic-clonic generalised (grand mal) epilepsy
   c) Generalised absence seizures (petit mal)
   d) Partial complex (psychomotor) seizures

3. Anticonvulsants should be withdrawn slowly to avoid:
   a) Ataxia and speech disorders
   b) Paradoxical stimulation
   c) Inducing seizures
   d) Hypertensive crisis.

4. Gingival hyperplasia is an adverse reaction of which one of these anti-epileptic drugs:
   a) Sodium valproate (Epilim ™)
   b) Vigabatrin
   c) Benzodiazepines
   d) Phenytoin

5. Visual field restriction is an adverse reaction of which anti-epileptic drug?
   a) Tiagabine, GABA reuptake inhibitor, for partial & generalized seizures
   b) Carbamazepine, blocks spread of seizures, blocks voltage dependent Na+ channels
   c) Vigabatrin, a GABA transaminase irreversible inhibitor
   d) Phenytoin, blocks spread of seizures, blocks voltage dependent Na+ channels

6. Magnesium sulfate is commonly used to prevent:
   a) Myoclonic seizures
   b) Eclampsia
   c) Focal seizures
   d) Febrile seizures

7. Antiepileptic agents stabilise the nerve cell membrane by altering the transport of:
   a) Sodium ions
   b) Potassium ions
   c) Calcium ions
   d) All of the above
8. Which of the following benzodiazepines is used to treat seizures?
   a) Nitrazepam
   b) Clonazepam
   c) Flunitrazepam
   d) Temazepam

9. The antiepileptic agent, vigabatrin, acts by:
   a) Facilitating the action of GABA
   b) Stimulating GABA receptors
   c) Inhibiting the reuptake of GABA
   d) Inhibiting the action of GABA transaminase.

10. Which of the following antiepileptic agents inhibit sodium channel functions?
    a) Phenobarbitone
    b) Phenytoin
    c) Vigabatrin
    d) All of the above

11. Which of the following is true of epilepsy in the elderly:
    a) The elderly do not get epilepsy, because neural transmission is slower.
    b) The elderly show secondary epilepsy, precipitated by stroke, systemic
diseases or chronic neurological conditions.
    c) The elderly are particularly prone to absence seizures.
    d) All of the above are true of epilepsy in the elderly.

12. Which of the following is true of epilepsy during a woman's lifespan
    a) Magnesium sulfate is used to treat the convulsions in eclampsia during
pregnancy.
    b) Epilepsy is more common in males but does occur in females.
    c) Antiepileptic drugs may cause contraceptive pill failure; hence, women of
childbearing age must take this into consideration.
    d) All of the above are true for epilepsy in females.

13. Which of the following is true of the aims of anticonvulsant therapy:
    a) Most patients with epilepsy require a combination of antiepileptic drugs to
prevent recurrent seizures.
    b) Most clients on anticonvulsants respond to monotherapy
    c) Patients who are diagnosed with epilepsy must adhere to a lifetime of drug
therapy.
    d) All of the above are true for antiepileptic drug treatment.

14. The effects of alcohol include all of the following except:
    a) Reduced eye/hand coordination
    b) Central nervous system depression
    c) Reduced visual acuity
    d) Central nervous system stimulation
15. Alcohol is purported to enhance the activity of which of the following neurotransmitters?
   a) Acetylcholine (muscarine)
   b) Gamma-aminobutyric acid (GABA)
   c) Norepinephrine
   d) Noradrenaline

16. Long-term effects on the cardiovascular system from excessive alcohol use include:
   a) Hypotension
   b) Vasoconstriction
   c) Cardiomyopathy
   d) None of the above

17. The secretions of which of the following hormones is/are lowered with excessive alcohol intake?
   a) Antidiuretic hormone
   b) Oxytocin
   c) Testosterone
   d) All of the above

18. Which of the following substances of abuse is a CNS stimulant?
   a) Inhalants (e.g. toluene, petrol, paint thinner, correction fluid)
   b) Alcohol
   c) Cocaine
   d) Benzodiazepines

19. Ingestion of foods containing tyramine may lead to a hypertensive crisis in persons taking
   a) A tricyclic antidepressant
   b) A selective serotonin reuptake inhibitor
   c) Lithium
   d) A nonselective monoamine oxidase inhibitor

20. Benzodiazepines enhance the effect of gamma-amino-butryric acid (GABA) on chloride ion channels by increasing
   a) The chloride conductance of each channel
   b) The frequency of channel opening
   c) The amount of time each channel remains open
   d) The affinity of chloride for the channel

21. The benzodiazepine which is converted to a more active metabolite with long duration of action is
   A. Diazepam, useful as an anti-convulsant
   B. Phenobarbitone, an adjunct in epilepsy
   C. Lithium, for preventing manic episodes
   D. Triazolam, for use in day procedures to reduce anxiety (anxiolytic)
11.3 Alcohol and Drug Abuse – Use your textbook, reference texts (Readings/Handouts) and other texts. Feedback is available on the subject website

True / False Questions Alcohol and Drugs of Abuse. Consult reference texts on pathophysiology Klaasen and Watkins (2010) or Paton and Touquet (2005) [download from the subject website]

1. Food intake does not affect the absorption of alcohol.

2. Alcohol is distributed throughout the water in the body, so that most tissues—such as the heart, brain, and muscles—are exposed to the same concentration of alcohol as the blood.

3. Heavy drinkers show higher blood concentrations of acetate on drinking a standard drink than a person who does not drink heavily, given the same standard drink.

4. The cytochrome P450 dependent microsomal ethanol oxidizing system is inducible by alcohol and explains the tolerance seen in heavy drinkers.

5. In the CNS, alcohol causes release of 5-hydroxytryptamine and dopamine and inhibits release of anti-diuretic hormone.

6. Even small doses of alcohol on a daily basis are harmful.

7. Alcohol is only eliminated by biotransformation in the liver.

8. The chronic toxicity effects of alcohol are limited the liver.

9. Acetaldehyde exposure is harmless as its product of oxidation, acetate, is readily excreted in urine.

10. Oxidative stress in the liver, caused by alcohol, can deplete glutathione levels.

11. The economic cost of drug misuse and abuse in Australia is mainly due to illicit drugs.

12. The vast majority of drug-related deaths in Australia are due to tobacco.

13. In opioid addiction, the long acting antagonist naltrexone is used.

14. Approximately 90% of ethanol is excreted unchanged by the kidneys.

15. Alcohol is not excreted into the milk of lactating women.
Summary of Session 11

See Unit “Drugs Affecting the Central Nervous System”, Chapter on “Anti-anxiety, Sedative and Hypnotic Drugs”
- Section on Key Background: Sleep and Anxiety.
- Summarize the pathophysiology and signs and symptoms of anxiety and insomnia

Benzodiazepines
These drugs are the most commonly prescribed drugs for the treatment of both anxiety and insomnia.
See Unit “Drugs Affecting the Central Nervous System”, Chapter on “Anti-anxiety, Sedative and Hypnotic Drugs”
- Section on Benzodiazepines.
- Summarize in your Drug Diary the pharmacodynamics, pharmacokinetics, adverse effects, drug interactions and warnings and contraindications of benzodiazepines

Treatment of Affective Disorders

There is no single factor identified as to the cause of affective disorders. These include depression, mania and bipolar disorder. A possible theory is that of the monoamine theory where an imbalance in the centrally acting catecholamine neurotransmitters are believed to be the cause.

See Unit “Drugs Affecting the Central Nervous System”, Chapter on “Psychotropic Agents”
- Section Treatment of Affective Disorders, up to Key Points

Depression

Depression can be divided into 3 main classes:
- major depressive disorder
- bipolar affective disorder
- dysthymia
- Summarize the pathophysiology, aetiology and signs and symptoms of depression

Drugs used for depression

There are 4 main groups of antidepressants:
- Tricyclic antidepressants (TCA)
- Selective Serotonin Reuptake Inhibitors (SSRIs) and Selective Noradrenaline reuptake Inhibitors (SNRI) and Noradrenaline Serotonin Reuptake Inhibitors (NSRI)
- Monoamine Oxidase Inhibitors (MAOI) and reversible inhibitors of monoamine oxidase
- Summarize in your Drug Diary the pharmacodynamics, pharmacokinetics, adverse effects, drug interactions and warnings and contraindications of TCAs, SSRIs, SNRI, MAOI and RIMA
Bipolar Disorder

Characterised by cyclic episodes of elation (mania) or depression and is associated with various behavioural features such as psychotic symptoms

☞ Summarize the pathophysiology, aetiology and signs and symptoms of bipolar disorder

☞ Summarize in your Drug Diary the pharmacodynamics, pharmacokinetics, adverse effects, drug interactions and warnings and contraindications of Lithium

Epilepsy

Describes a group of neurological disorders characterised by recurrent sporadic episodes of convulsive seizures.

☞ See Unit “Drugs Affecting the Central Nervous System”, Chapter on “Anti-epileptic Drugs”

☞ Summarize the pathophysiology, aetiology and signs and symptoms of epilepsy

There are 3 main groups of anti-epileptic drugs, AEDs could

☞ enhance GABA-mediated inhibition of neural activity
☞ inhibit sodium channel function, thus blocking repetitive depolarisation of neurons
☞ miscellaneous

☞ Summarize in your Drug Diary the main indications, pharmacodynamics (M of A) and ADR of Barbiturates, Phenyoitn, Topiramate, Sodium valproate and Gabapentin

Schizophrenia

Manifested by disordered mood, thought, perception and volition leading to delusion, withdrawal and loss of insight.

☞ See Unit “Drugs Affecting the Central Nervous System”, Chapter on “Psychotropic agents”

☞ Section on Antipsychotic Agents up to Conventional (typical) antipsychotics

☞ Summarize the pathophysiology, aetiology and signs and symptoms of schizophrenia

The typical and atypical antipsychotic drugs are used to treat this disorder

☞ Summarize in your Drug Diary the pharmacodynamics (M of A), pharmacokinetics, adverse effects, drug interactions and warnings and contraindications of typical and atypical antipsychotic drugs

Parkinson’s disease (Covered in Session 12)

Progressively debilitating disorder of the basal ganglia, characterised by tremor at rest, bradykinesia, forward flexion of the trunk, muscle rigidity, loss of postural reflexes and weakness.

☞ See Unit “Drugs Affecting the Central Nervous System”, Chapter on “Drugs for Neurodegenerative Disorders…..”

☞ Section on Parkinson’s Disease up to Monographs on Levodopa-Carbidopa

☞ Summarize the pathophysiology, aetiology and signs and symptoms of Parkinson’s disease

☞ Summarize in your Drug Diary the pharmacodynamics, pharmacokinetics, adverse effects, drug interactions and warnings and contraindications of Levodopa (L-Dopa) - Carbidopa

CNS depressants

Alcohol is a CNS depressant with multiple effects across body systems

☞ See Unit “Drugs Affecting the Central Nervous System”, Chapter on “Drug Dependence and Social Pharmacology”

☞ From a pathophysiology text e.g. Kumar & Clark (eds) (2013), Research Alcohol in Chapter 5 “Nutrition” thiamine deficiency and section on Alcohol and Chapter 22 “Neurological Disease” look for the section on Toxic neuropathies (Jarman, 2013)

☞ Summarize the toxic effects and toxicokinetics of alcohol
Additional Resources

If you find other educationally-useful videos, add them to the Loop / forums

- From a pathophysiology text eg Kumar & Clark (eds) (2013), Research Alcohol in Chapter 5 “Nutrition” thiamine deficiency and section on Alcohol and Chapter 22 “Neurological Disease” look for the section on Toxic neuropathies (Jarman, 2013)

Revision Questions / Activities from the Reading Guide:

1. Which neurotransmitter do benzodiazepines act upon?
2. Benzodiazepines have different half lives. How is this used therapeutically and give examples of the indications for this?
3. Outline the adverse effects of Benzodiazepines, BZD
4. Compare and contrast TCAs, SSRIs and MAOI (Include Mechanism of Action, adverse effects and indications and give an example of each). TCA = T___-C_____ depressants, SSRI = S________ S________ R__________ Inhibitors, MAOI = M___-A_____-O_________ase Inhibitors
5. What is the drug of choice in the treatment of bipolar affective disorder?
6. Outline some of the adverse effects of Lithium and explain why these happen?
7. Give the three therapeutic classes of anti-epileptic drugs and give examples of AEDs (Anti-E_____ Drugs) from each class.
8. What advantage do the atypical have over the typicals in the treatment of Schizophrenia?
9. What is the Mechanism of Action of carbidopa and how does it improve the efficacy of Levodopa?

Answer the following:

From Bryant & Knights (2015)

- Review questions: Antianxiety, Sedative & Hypnotic Drugs; Anti-epileptic Drugs; Psychotropic Agents; Drug treatment of Parkinson’s disease, Drugs used in Migraine & other Headaches; CNS Depressants (Alcohol)