

## **DUAL DIAGNOSIS SUPERVISION GROUP**

### **“Illicit Drugs and Drug Interactions”**

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#### **PLAN OF SESSION**

**Specific research on drug interactions between street and prescribed drugs is not routinely done! Therefore we tend to rely on case reports.**

1. Look at what is going on in the brain when we take illicit drugs. Also look at the effects of common street drugs so we can match the drug up to the receptors being activated.
2. Look at the ways in which prescribed/non-prescribed drugs interact in the body.
3. Look at examples of drug (prescribed/illicit) interactions.
4. We will then have the basic information we need to be able to predict what sort of drug interactions we might see from common drug combinations!!
5. Case examples:
  - to think of the possible drug interactions that may occur
  - and strategies for how we can manage them alongside the client!

# PATHWAYS

## Dopamine Pathways

Nerve pathways which use dopamine to communicate are “dopaminergic”.

Dopamine is said to be “the link between movement and madness”.

We will consider 2 of the dopamine pathways:-

1. Nigrostriatal dopamine pathway – this enables us to perform smooth movements. (This is the pathway which is malfunctioning in Parkinson’s disease – hence patients with Parkinson’s find moving a very stiff and slow experience – they also experience a tremor).

Also note that when psychiatrists prescribe antipsychotic medication, these tend to block dopamine – but we do not want to switch off dopamine altogether in the nigrostriatal pathway or we will cause the patient significant movement problems (extrapyramidal side effects).

2. Mesolimbic dopamine pathway – when activated, this is responsible for:-

- Pleasure sensations
- Behaviours – the pleasure-reward system
- Euphoric effect

An excess of dopamine in this pathway causes:-

- Hallucinations
- Delusions (often of paranoid type)
- Schizophrenia-like illnesses.

Stimulant street drugs (amphetamine, cocaine, crack, methamphetamine) act on this system.

## Serotonin Pathways

These are “serotonergic” and use serotonin to communicate. Remember that the serotonin system is often targeted by antidepressant medications! Especially the “SSRI” group of antidepressants (selective serotonin reuptake inhibitors), which cause a significant increase in serotonin levels in the brain.

Ecstasy has an effect on this system.

Serotonin pathways regulate:-

- Body temperature
- Cognitive function (ability to thrive)
- Regulate emotions – including panic and anxiety

- Regulate appetite and satiety (fullness)
- Sleep-wake cycle
- Sexual functioning (patients taking SSRI's often have difficulty achieving erection and/or orgasm)

An excess of serotonin causes:-

- Increased body temperature
- Increased heart rate
- Anxiety
- Panic
- Confusion ⇒ coma ⇒ death
- Sweating
- Shivering
- Nausea
- Twitching ⇒ hyperreflexia ⇒ seizures

Patients on high doses of SSRI's often feel very sweaty. We are cautious when prescribing more than one type of antidepressant to a patient as we increase the risk of unpleasant side effects and "serotonin syndrome".

### **Noradrenergic Pathways**

This is part of the sympathetic nervous system and is important in enabling our "fight or flight" response. It puts us in a state of "readiness", on full alert to escape or fight danger.

- Increased blood pressure
- Increased heart rate
- Blood diverted from skin to skeletal muscles to enable us to run!
- Peripheral blood vessels narrow in order to move the blood to muscles.

Stimulant street drugs have a sympathomimetic action ie they mimic the effect of adrenaline on this system.

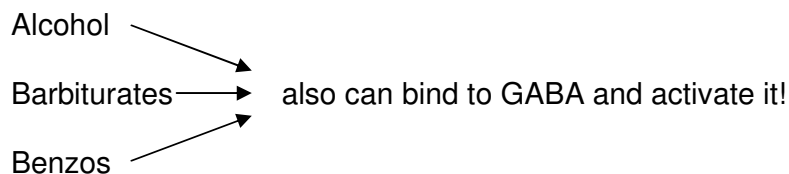
## Nerves which respond to GABA (GABA-ergic)

GABA (gamma-aminobutyric acid) is the major “calming” transmitter in the brain.

Activating GABA leads to:-

- Decreased anxiety
- Relaxation
- Sedation, coma, death (in excess)

Natural GABA binds to GABA receptor



Benzodiazepines, barbiturates and alcohol lead to GABA activation.

## Opiate Receptors (named after Greek alphabet Mu - $\mu$ , Kappa - $\kappa$ , Delta - $\delta$ )

Mu – the main opiate receptor for morphine-like opiates, including heroin.

Activation of Mu lead to:-

- Pain free, comfortable
- Sedation, sleepy + relaxed – coma in excess
- Reduces physical + psychological pain

Mu in turn triggers dopamine release  $\Rightarrow$  makes you feel high (see the euphoriant effect in the dopamine system).

Heroin acts on Mu receptors.

## Heroin alone causes:-

Brief period of euphoria (pleasure/rush), then 4 hours of lethargy

- Feel warmth and well-being
- Sleepy and relaxed – drowsy “on the nod”
- Skeletal muscle of neck particularly relaxed!
- Analgesia
- Nausea & vomiting
- Pinpoint pupils
- Dry mouth
- Itching
- Sweating
- Reduced cough reflex – more likely to inhale vomit
- Respiratory depression
- Hypothermia
- Low blood pressure
- Constipation
- REM sleep suppressed (and sleep pattern likely to remain disturbed for long time after)

Heroin commonly “cut” with:-

- Sugar
  - Baking soda
  - Talc
  - Starch
  - Nutmeg
  - Curry powder
  - Brick dust
  - Ajax, Vim
  - Quinine (less so now) ⇒ affects eyesight!
  - Crushed benzos or paracetamol ⇒ sedation from benzo ⇒ overdose risk
- potential interactions!
- 
- A diagram consisting of three arrows pointing from the list of substances to the text 'potential interactions!'. One arrow points from 'Sugar', another from 'Nutmeg', and a third from 'Crushed benzos or paracetamol'.

Heroin acts on the Mu receptors.

## Benzodiazepines cause:-

- Anxyolytic
- Sedation (coma, death)

Cut with:-

- May be “fake” from internet.

Benzos act on the GABA receptors.

### **Alcohol causes:-**

- Sociable chatty feeling (small amounts)
- Progressive sedative effects

(NB stimulants do not reverse alcohol-related performance deficits)

Alcohol acts on the GABA receptors.

### **MDMA, Ecstasy causes:-**

- Gives energy buzz
- Feel alert & alive
- In tune with surroundings
- Great love for those around you
- Tightening of jaw muscles/teeth grinding
- Increased body temperature
- Increased heart rate
- Anxiety, panic
- Confusion
- (paranoia)
- Feel very “down” afterwards

“E” cut with:-

- Sorbitol
- Caffeine
- Speed may be found in “fake ecstasy” tablets

E acts on the serotonin pathway (and also on dopamine)

### **Amphetamines/Cocaine/Crystal Meth cause:-**

- Feel wide awake, excited, aroused, exhilarated
- Feeling of energy – dance/activity for hours
- Increased heart rate
- Increased blood pressure
- Narrowing of blood vessels

In excess:-

- Strain on heart
- Increased blood pressure – ruptures blood vessels in brain, stroke
- Panic and anxiety
- Aggression
- Irritable
- Psychosis
- Overheating – increase in body temperature
- Cocaine increases heart attack risk x 24
- Increase in libido (esp crystal meth), increase or decrease in libido with cocaine
- Convulsions

- Fit/stroke/heart attack – even in young fit men.
- (mood – crashing low after)

Mixture of dopamine excess and adrenaline excess. They also cause increased release of serotonin and noradrenaline ie all monoamines are increased. Therefore do not give MAOI antidepressant to someone who is a stimulant user as there is risk of serotonin ↑↑↑!

Cut with:-

- Caffeine
- Sugar
- Paracetamol
- Starch

Stimulants act on the dopamine and noradrenaline pathways.

## Ways in which drugs could interact (whether prescribed or illicit)

### 1. Liver level

Drugs are cleaned out of our body by the liver (usually).

Liver uses enzymes to “chew up” drugs for body to eliminate.

Some drugs cause the liver enzymes to SPEED UP

eg Rifampicin, smoking nicotine/tobacco/cannabis/St John’s Wort

Therefore liver chews faster through other drugs which need those enzymes for their own breakdown. Therefore end up with a lesser dose in your body because the drug is being removed faster.

Eg client on Methadone maintenance admitted to hospital and prescribed Rifampicin (an antibiotic)

Rifampicin causes the liver to speed up and so the Methadone is also metabolised and eliminated quicker. The client then experiences opiate withdrawals – but the staff are suspicious that the client is “after more Methadone”. So, we need to explain the drug interaction that is happening and increase the Methadone dose for the duration of the course of Rifampicin antibiotic (this client needed his dose of Methadone increasing by about 1/3 extra).

Eg smoking cannabis resin in cigarette (nicotine) + Clozapine

Remember, nicotine speeds up liver enzymes. Clozapine is an antipsychotic drug with a sedative side effect. Patient was stable and alert when he was a smoker – but when he decided to quit smoking, the liver slowed down to normal levels and did not clear the Clozapine as quick! Therefore, he became sedated as his body got an effectively bigger dose of Clozapine once it was no longer being metabolised as quick!!

### 2. Nerve ending receptor

a) 2 drugs acting on same receptor eg alcohol and benzos

both act on GABA

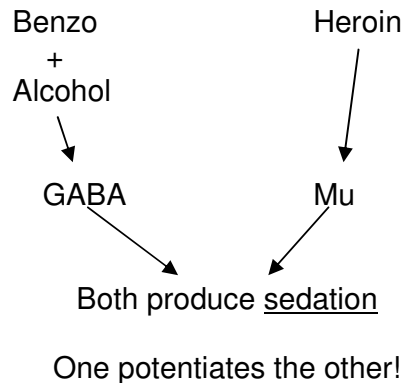
= additive effect

More likely to experience effects of excess GABA activation (risk of oversedation ⇒ coma ⇒ death).



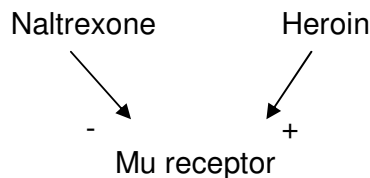
b) 2 drugs, each acting on different receptors with similar overall effect

Eg



Interaction at receptors can be antagonistic

Eg



Naltrexone displaces heroin and wins the competition for the Mu receptor.

But if lots and lots of heroin, heroin can out-compete Naltrexone, therefore big overdose risk!)

### Examples of Drug Interactions

1. Patient on antipsychotic (which blocks dopamine) who takes amphetamine on occasion. No psychotic symptoms complained of and requests to come off the antipsychotic.

Q. What might we see? A. A return of psychosis!

Antipsychotic may be covering up symptoms of psychosis which become apparent once the drug is withdrawn.

2. Using cannabis and cocaine may enhance onset of action – cannabis induced vasodilation of nasal mucosa, which enables easy absorption of cocaine snorted into the nasal passage.

3. Ecstasy (which stimulates serotonin) + Moclobemide (an antidepressant which increases monoamine and serotonin availability) – 4 deaths with serotonin toxicity

4. Patient who regularly uses Ecstasy, sees GP about low mood, but fails to tell GP about Ecstasy use. GP prescribes SSRI.

Q. What interaction might occur? A. Patient is at risk of serotonin toxicity as both Ecstasy and SSRI act on the serotonin system.

5. Patient on Dexamphetamine for ADHD, felt depressed and GP prescribed SSRI ⇒ risk of serotonin syndrome!
6. Patient with alcohol dependency, sees GP with persistent low mood, requests something to “pick me up”. GP prescribes Dothiepin (a sedative tricyclic antidepressant). When patient intoxicated and disinhibited on alcohol, takes impulsive overdose of the antidepressant.

Q. What interaction might occur? A. Dothiepin is a sedative drug which, in the presence of alcohol (also a sedative) can cause an increased risk of death in overdose.

7. Poppers (Amyl nitrate) – causes decrease in blood pressure (lightheaded) plus Viagra (Sildenafil) ⇒ potentially fatal decrease in blood pressure.
8. Alcohol is involved in more deaths by overdose than any other single drug.

Most die of respiratory failure.

Alcohol causes an increase in (sedative) inhibitory effect of GABA ⇒ slows and stops breathing.

### Heroin overdose

- Single unemployed men in late 20's/early 30's long history of opiate dependence
- Often alcohol or benzo use
- Recently reduced tolerance (prison)
- No evidence of toxicity from contaminants eg street heroin

The following will increase risk of overdose/death:-

- Heroin in combination with
- Sedative antidepressants (not SSRIs)
  - Alcohol
  - Benzodiazepines
  - Other opiates

9. Dual diagnosis patients with psychotic disorders
  - Opiates thought to have some (weak) antipsychotic properties – “self-medicating” with heroin! ie heroin is augmenting our treatment! (People using heroin alone tend not to develop psychosis!)
  - Can use depot (typicals or LAI Risperidone) to treat the psychosis.
  - Oral atypicals or typicals – even Clozapine (sedative) can be used to treat the psychotic illness.
  - Clozapine in dual diagnosis “well documented that Clozapine has direct effect on reducing substance use in this population”.

### Risk of antipsychotic induced fatal arrhythmia

Lots of individual patient factors affect the degree of risk for having an arrhythmia

- Old
- Physically unwell
- Large doses medication
- Using illicit drugs

BIG RISK FACTORS we pay attention to are

- Heart defect
- QTC prolongation
- Family history of sudden cardiac death
- Heart failure, arrhythmia

Alcohol and drugs are “secondary risk”.

Signs of arrhythmia

- Short of breath
- Dizzy
- Palpitations
- Loss of consciousness

If there are risks identified, then the advice is to check ECG:-

- Baseline ECG for patients starting antipsychotics
- Again 2 weeks after starting
- Again at 6 monthly intervals

High Risk of Arrhythmia	Medium Risk of Arrhythmia	Low Risk of Arrhythmia
CPZ	Amisulpride	Aripiprazole
Droperidol	Clozapine	Olanzapine
Haloperidol	Quetiapine	Trifluoperazine
Thioridazine	Risperidone	

**Information Sources:-**

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