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Foundations of Ketamine-Assisted Psychotherapy

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NOVAMIND

Module 3

What is Ketamine?

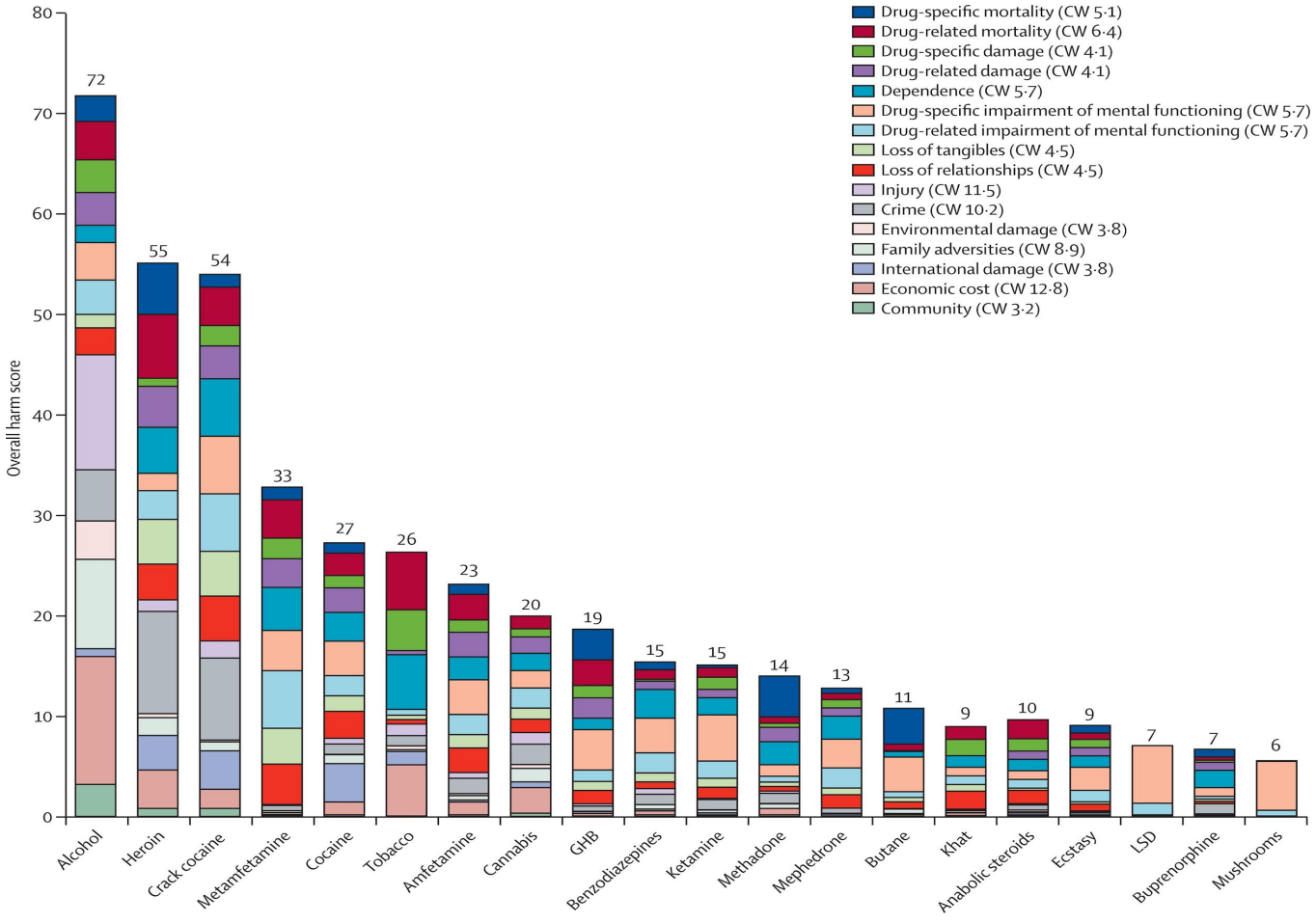
Module 3

Lesson 3.7

Medical & Safety Considerations

Psychedelics & Mental Health

- Decreased rates of suicide and psychological distress among those reporting prior use of psychedelics (Hendricks 2015)
- No evidence of increased rates of mental health problems (Krebs 2013)
- Cases of mental health complications following a psychedelic are rare (<0.1%), even in vulnerable populations (<0.2%), and rarer still with proper screening (Cohen 1962, Studerus 2011)
- Studies examining use patterns in humans & self-administration in animals suggests that classic psychedelics possess little or no abuse liability (Nichols 2004)
    - Rhesus monkeys found LSD to be aversive, working to avoid a cue associated with LSD infusion (Hoffmeister 1975).
        - There is no human LSD dependence syndrome, despite its availability for many decades
    - Psilocybin failed to produce consistent self-administration in rodents or monkeys (Fantegrossi, Woods et al. 2004; Nichols 2004)


Overall harm score
80
70
60
50
40
30
20
10
0
72
55
54
33
27
26
23
20
19
15
15
14
13
11
9
10
9
7
7
6
Alcohol
Heroin
Crack cocaine
Metamfetamine
Cocaine
Tobacco
Amfetamine
Cannabis
GHB
Benzodiazepines
Ketamine
Methadone
Mephedrone
Butane
Khat
Anabolic steroids
Ecstasy
LSD
Buprenorphine
Mushrooms
Drug-specific mortality (CW 5·1)
Drug-related mortality (CW 6·4)
Drug-specific damage (CW 4·1)
Drug-related damage (CW 4·1)
Dependence (CW 5·7)
Drug-specific impairment of mental functioning (CW 5·7)
Drug-related impairment of mental functioning (CW 5·7)
Loss of tangibles (CW 4·5)
Loss of relationships (CW 4·5)
Injury (CW 11·5)
Crime (CW 10·2)
Environmental damage (CW 3·8)
Family adversities (CW 8·9)
International damage (CW 3·8)
Economic cost (CW 12·8)
Community (CW 3·2)

And yet...

It’s really important that our enthusiasm and hope for the future do not overshadow the need to consider:

- ➔ Optimal conditions
- ➔ Contraindications
- ➔ Psychospiritual emergencies
- ➔ Safety considerations & prohibited medications

MDMA-Assisted Psychotherapy: Participants in Studies agree to:

- Attempt to maintain a steady amount of social support external to their psychotherapy session
- NPO except liquids after midnight prior to dosing session
- No caffeine or nicotine at least 2 hours before and 6 hours after dosing
- No new medications or supplements without study team approval (other than tylenol & ibuprofen)
- Willing to be driven home from dosing session
- 2 forms of contraception

MDMA Studies: Sample exclusion Criteria

- Comorbid mental health conditions:
  - Psychotic disorders (including immediate family member with psychosis)
  - Bipolar disorder
  - Dissociative identity disorder
  - MDD with psychosis
  - Eating disorder with active purging
  - Suicidality (current serious suicide risk)
  - Certain personality disorders (i.e. Schizoid, Schizotypal, Paranoid)
- Cardiac
  - Personal or family history of sudden or early life cardiac even (1st and 2nd degree relatives included)
  - Poorly controlled hypertension (>140/90 mmHg on 3+ occasions)
  - Cardiac arrythmias (other than occasional PVCs)
  - QTc > 450ms, or any risk of Torsades (CHF, hypokalemia, family hx of long QT)
- Medications
  - Use of SSRIs / SNRIs within 3 months prior to study
  - Taking medications that prolong QT interval
- Any other significant medical or laboratory abnormality deemed by study team to be a contraindication

General Contraindications for Psychedelic Medicine

- Medical or psychological fragility
- Certain medications (more on that later - save to say it's important to examine this from both perspectives)
- Lack of social support, including around medicine use; low socioeconomic status; housing issues

"So um, I guess whoever you see with the most fragile mind, ah so there's a different level of, of fragile mind even in the population we're choosing to serve. You can always see where that, maybe I can't help that person, oh everyone here is fragile, but that person right there is probably too fragile to even make it through, so just gauging those things." ~Ayahuasca ceremonial leader

Antidepressant	Phenethylamines -MDMA, mescaline	Tryptamines -Psilocybin, LSD	MAOI-containing -Ayahuasca, Syrian Rue	Ketamine	Ibogaine
SSRIs · Paroxetine (Paxil) · Sertraline (Zoloft) · Citalopram (Celexa) · Escitalopram (Lexapro) · Fluxoetine (Prozac) · Fluvoxamine (Luvox) **SPARI** · Vibryyd (Vilazodone) · Trintellix (Vortioxetine) **SNRI** ·Venlafaxine (Effexor) ·Duloxetine (Cymbalta) ·Desvenlafaxine (Pristiq) ·Levomilnacipran (Fetzima)	Taper & discontinue at least 2 weeks prior (all except fluoxetine) or 6 weeks prior (fluoxetine only) due to loss of psychedelic effect MDMA is unable to cause release of serotonin when the serotonin reuptake pump is blocked. This leads to drastically reduced effects [1-7]	Consider taper & discontinuation at least 2 weeks prior (all except fluoxetine) or 6 weeks prior (fluoxetine only) due to potential loss of psychedelic effect Chronic antidepressant use may result in down-regulation of 5HT2A receptors and blunted psychedelic experiences [8, 9]. This does not seem to affect psilocybin for some	Taper & discontinue at least 2 weeks prior (all except fluoxetine) or 6 weeks prior (fluoxetine only) due to potential risk of serotonin syndrome Life threatening toxicities can occur with these combinations and is strictly contraindicated [10, 11]	Has been studied and found effective both with and without concurrent use of antidepressants Recommended to be used in conjunction with oral antidepressants by esketamine manufacturer	Taper & discontinue at least 2 weeks prior (all except fluoxetine) or 6 weeks prior (fluoxetine only) due to risk of additive QTc interval prolongation, arrhythmias, or cardiotoxicity Some antidepressants are liver (CYP2D6) inhibitors and have been shown to double ibogaine blood concentrations [12]
DNRI · Bupropion (Wellbutrin)	Increased effects of MDMA with higher blood concentrations for longer [13]. May increase risk of seizures in combination. Caution in combination. Consider taper & discontinuation of bupropion. Alternatively, a 25% reduced dose of MDMA if bupropion is continued.	Loss of effect not predicted to occur, consider taper & discontinuation depending on goals of psychedelic use	Taper & discontinue at least 2 weeks prior due to potential of adverse effects, however serotonin syndrome unlikely to occur [14]		Taper & discontinue at least 2 weeks prior to use. May increase risk of seizures in combination. CYP2D6 inhibitor with potential to increase ibogaine blood cocnentrations
· Mirtazapine (Remeron)	Taper & discontinue at least 2 weeks prior due to loss of psychedelic effect Mirtazapine does not block the serotonin reuptake pump like SSRI, SPARI, or SNRI antidepressants. It blocks the 5HT2A receptor, thus is predicted to cause a blunting or loss of psychedelic effects. It has not been associated with serotonin syndrome with MAOIs [14]				Taper & discontinue at least 2 week prior due to risk of additive QTc interval prolongation, arrhythmias, or cardiotoxicity

SSRI = selective serotonin reuptake inhibitor SPARI = serotonin partial agonist and reuptake inhibitor SNRI = serotonin norepinephrine reuptake inhibitor DNRI = dopamine norepinephrine reuptake inhibitor MAOI = monoamine oxidase inhibitor SERT = serotonin reuptake pump 5HT2A = serotonin 2A receptor

Antidepressant	Phenethylamines -MDMA, mescaline	Tryptamines -Psilocybin, LSD	MAOI-containing -Ayahuasca, Syrian Rue	Ketamine	Ibogaine
Tricyclic Antidepressant (TCA) · Amitriptyline (Elavil) · Nortriptyline (Pamelor) · Clomipramine (Anafranil) · Imipramine (Tofranil) · Desipramine (Norpramin) · Chlorpheniramine	Taper & discontinue at least 2 weeks prior due to loss of psychedelic effect MDMA is unable to cause release of serotonin when the serotonin reuptake pump is blocked. This leads to drastically reduced effects	Consider taper & discontinuation at least 2 weeks prior due to potential intensified effects Chronic TCA use was reported to increase the subjective effects of LSD [15]	Taper & discontinue at least 2 weeks prior due to potential risk of serotonin syndrome. Risk is highest with clomipramine, imipramine, and chlorpheniramine [14] Life threatening toxicities can occur with these combinations and is strictly contraindicated	Has been studied and found effective both with and without concurrent use of antidepressants Recommended to be used in conjunction with oral antidepressants by esketamine manufacturer	Taper & discontinue at least 2 weeks prior due to risk of additive QTc interval prolongation, arrhythmias, or cardiotoxicity Some antidepressants are liver (CYP2D6) inhibitors and have been shown to double ibogaine blood concentrations
· Trazodone (Desyrel)	Taper & discontinue at least 5 days prior due to loss of psychedelic effect Trazodone blocks 5HT2A receptors at lower doses (25-150mg) and starts blocking the serotonin reuptake pump (SERT) at >150mg [14]. It has an active metabolite that also blocks 5HT2A receptors as well as modulating many other 5HT receptors				Taper & discontinue at least 1 week prior due to risk of additive QTc interval prolongation, arrhythmias, or cardiotoxicity
· Buspirone (Buspar)	Taper & discontinue at least 5 days prior due to loss of psychedelic effect Buspirone is a non-psychedelic partial agonist at serotonin receptors, thus may display blunting of psychedelic effects due to competitive inhibition when used in combination with psychedelics [16]. It does not inhibit the reuptake of nor release neurotransmitters, thus risk of serotonin syndrome with MAOIs is low				Taper & discontinue at least 5 days prior due to potential risk of toxicity
MAO-A Inhibitors* · Phenelzine (Nardil) · Isocarboxazid (Parnate) · Tranylcypromine (Marplan) · Moclobemide *chronic use	Taper & discontinue at least 2 weeks prior due to potential risk of serotonin syndrome or hypertensive crisis [17]	Consider taper & discontinuation at least 2 weeks prior due to potential loss of psychedelic effect [15] Contraindicated with tryptamine 5-MeO-DMT [18, 19]	Taper & discontinue at least 2 weeks prior Additive use of MAOIs may cause intensified experiences or cardiovascular collapse (fainting or dangerously low blood pressure)		Taper & discontinue at least 10 days prior due to potential risk of toxicity [20]
MAO-B inhibitors · Selegeline (Emsam)	Intensified effects, risk of serotonin syndrome at doses ≥9mg/day Taper & discontinue at least 2 weeks prior, especially if dose ≥9mg/day	Intensified effects possible, risk of serotonin syndrome at doses ≥9mg/day with 5-MeO-DMT; psilocybin or LSD likely have low risks of physical toxicity in combination			

Thanks for listening!

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