ALTERNATIVE PAIN MANAGEMENT IN DIGITAL MEDIA

From Arnica to LSD

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Reality of pain management

- Even the best available treatments are not effective in all patients (Borsook et al., 2013)
- The most effective monotherapies have only 30% efficacy
- The numbers-needed-to-treat with monotherapy to achieve pain reduction of at least 50% are in the range of 2 to 4 (Braune, 2004)
- Potential benefit from combination therapy or individualized pain management (Jannetto et al., 2011; Kasai et al., 2011)
- Most patients do not have access to such level of care!

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Is there any treatment for arthritis in homeopathy? V Does homeopathy work for back pain? \sim What is Ruta used for in homeopathy? \sim Is homeopathic medicine effective for arthritis? \sim

Feedback

Homeopathy for Pain Management - Mary Ann Liebert, Inc. https://www.liebertpub.com/doi/full/10.1089/act.2017.29129.ble

What is homeopathy?

- Used by over 2% of the U.S. population (Dossett et al., 2018)
- A system of alternative medicine
- Claim: a substance that causes the disease in healthy people would cure same disease in sick people
- Homeopathic preparations are manufactured using a process of homeopathic dilution well past the point where no molecules of the original substance remain

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Pain

Dr Ronald Livingston discusses the homeopathic approach •

Pain is perhaps the most widespread and arresting symptom individual homeopathic medicines.

Defined in the Oxford Dictionary as "suffering or distress", it c discomfort or unpleasantness, soreness, tenderness and acr

Much attention is given nowadays in pain clinics to the under contains nerve paths concerned predominantly either with m are concerned. Physiologists sub-divide the two types of pair conveyed through different pathways in the nervous system.

- Conditions in which pain shoots along a limb respond to Hypericum
- Causalgia, or the pain experienced at the site corresponding to that of an amputated limb, is often helped by Chamomilla
- Arsenicum album where the pain is of a burning character
- Cardiac pain...responds to Cactus grandiflorus and Latrodeatus mactans
 - Opium which is used homeopathically for the absence of pain...
 Opium is also useful for the physical pain we understand as fear
 as in nightmares when the terror returns again and again, night after night, often for years

The ordinary approach to this is highly material, even when concerned with matters of the emotions and the mind. We are all accustomed to describe

Evidence?

- First meta-analysis of homeopathy to treat <u>fibromyalgia</u> found significant improvements in tender-point count, pain intensity, and fatigue compared to placebo (Boehm et al., 2014)
- These results were disproven by methodologically more sound study rendering the effectiveness of homeopathy as a symptomatic treatment for <u>fibromyalgia</u> unproven (Perry at al., 2017)
- Homeopathy did not appear to be superior to placebo in patients suffering from acute painful episodes of <u>knee osteoarthritis</u> (Koley et al., 2015) or <u>dysmenorrhea</u> (Alizadeh et al., 2015)
- Potentized estrogen was significantly more effective than placebo for reducing endometriosisassociated <u>pelvic pain (Teixeira et al., 2017)</u>
- Both individualized homeopathy and combination products have shown benefit in reducing chronic low back pain (Beer et al., 2017)
- Reduction of NSAID and opioid use in patients with musculoskeletal pain who were prescribed homeopathic preparations by their physicians (Danno et al., 2014)

Pharmacology

- Some of the plants used in homeopathy do have analgesic properties
- Hypericum perforatum induces antinociception, relieves from acute and chronic hyperalgesia states and augments opioid analgesia (Galeotti, 2017)
- Arnica montana may represent a valid alternative to non-steroidal antiinflammatory drugs (Janniti et al., 2016)
- IMPORTANT: <u>dosages</u> used in these studies are <u>multiple orders of magnitude higher</u> than in homeopathic preparations

GUESS THE DRUG

- NMDA receptor antagonist
- Ligand of the μ -, κ -, and δ -opioid receptors
- Sigma σ 1 and σ 2 receptor agonist
- Partial agonist of the high-affinity state of the dopamine D2 receptor
- Ligand of the serotonin 5-HT2A receptor
- Potentiator of the serotonin 5-HT3 receptor
- Muscarinic acetylcholine receptor antagonist
- Negative allosteric modulator of nicotinic acetylcholine receptors
- Ligand of the estrogen receptor $\mathsf{ER}\alpha$
- Inhibitor of cholinesterase
- Inhibitor of the reuptake of serotonin, norepinephrine, and dopamine
- Ligand of the PCP site 2
- Blocker of voltage-gated/dependent sodium and calcium channels
- Blocker of HCN1 cation channels
- Inhibitor of nitric oxide synthase
- Indirect agonist of the AMPA receptor

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Ketamine vs. Phencyclidine

- Compared with ketamine, phencyclidine proved to be similarly selective as an NMDA receptor antagonist but approximately 10 times more potent and longer lasting following either local or systemic administration (Lodge and Anis, 1982; Anis et al., 1983)
- Provide anaesthesia and analgesia without causing cardiorespiratory depression
- When used as a sole anaesthetic drug patients sometimes experience psychosis, agitation, and dysphoria post-operatively
- Unlike the weeks of therapy required for SSRI and SNRI, mood is elevated rapidly after single injections of ketamine which provide relief for days and even weeks (Aan Het Rot et al., 2012; Caddy et al., 2014; Duman, 2014)
- Dosage: neuroprotective vs. neurotoxic effect (Olney et al., 1989)

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My Adventures With the Trip Doctors - The New York Times https://www.nytimes.com/.../health-issue-my-adventures-with-hallucinogenic-drugs-med...

May 15, 2018 - The researchers and renegades bringing **psychedelic** drugs into the ... out there again, but this **time** spread over the landscape like **paint**, ...

How Psychedelic Drugs Can Help Patients Face Death - The New ... https://www.nytimes.com/.../how-psychedelic-drugs-can-help-patients-face-death.html

Apr 20, 2012 - They're a new way to approach the most dire time of life. ... Grof kept careful notes of his many **psychedelic** sessions, and in his various papers The best **of The New York Times** Magazine delivered to your inbox every week, in a lower key but whose lives are clearly compromised by their chronic **pain**?

How Does a Writer Put a Drug Trip Into Words? - The New York Times

https://www.nytimes.com/2018/12/24/.../psychedelics-how-to-change-your-mind.html

Dec 24, 2018 - William James famously wrote that mystical experience - perhaps the closest

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Why Did My Grandmother Try LSD for Multiple Sclerosis in ... - Forbes https://www.forbes.com/.../why-did-my-grandmother-try-Isd-for-multiple-sclerosis-in-... •

Aug 4, 2015 - But I don't find much about using **LSD** for multiple sclerosis (MS), ... and **pain**—which is a key feature of multiple sclerosis—others are a tad ...

Do Psychedelics Drive You Crazy Or Keep You Sane? - Forbes https://www.forbes.com/sites/.../do-psychedelics-drive-you-crazy-or-keep-you-sane/ •

Mar 11, 2015 - **Psychedelic** drugs such as **LSD**, psilocybin (found in "magic mushrooms"), and mescaline (the active ingredient in peyote) were once called "psychotomimetic" because they were said to simulate the symptoms of schizophrenia. At first that purported quality inspired hope that ... Missing: pain | Must include: pain

Psychedelic Retreats And The Future Of Mental Health: A ... - Forbes https://www.forbes.com/.../psychedelic-retreats-and-the-future-of-mental-health-a-revi... •

Nov 30, 2018 - A personal look at psychedelics and the future of therapy. Missing: pain | Must include: pain

Scientists Rethink Psychedelics As Attitudes Change Toward ... - Forbes

https://www.forbes.com/.../scientists-rethink-psychedelics-as-attitudes-change-toward-f... Jan 31, 2019 - The generation who brought **psychedelic** drugs to the attention of the ... 3D rendering of human face morphed with fractal **paint** suitable as a ...

Trial Shows New Opioid Alternative Could Be Less Addictive - Forbes https://www.forbes.com/.../positive-results-for-cara-therapeutics-pain-drug-cr845-in-h... •

Oct 29, 2014 - In fact, much of our differences in **pain** tolerance are due to our emotional reaction to **pain**. ... Do people who like **hallucinogens** like CR845?

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HEALTH | By Suzannah Weiss | May 22 2018, 4:16pm

People Are Drinking Ayahuasca to Treat Physical Illnesses

Could the psychedelic be changing people's perceptions of pain?





Lysergic acid diethylamide (LSD) and psilocybin

- May be beneficial for depression and anxiety associated with distress in life-threatening diseases
- 5-hydroxytryptamine (5-HT) receptor agonists and may interact with nociceptive and antinociceptive processing which implies their potential use in patients with persistent pain (Whelan et al., 2018)
- Psilocybin and LSD in non-hallucinogenic doses were comparable to or more efficacious than most conventional medications in treatment of cluster headache (Schindler et al., 2015)
- Safe if administered by a healthcare professional
- Microdose: 5 20 mcg vs 100 mcg LSD
- Dosage, dosage, dosage!!!

Salvinorin A

- An active principle of Salvia divinorum
- The first reported non-nitrogenous (non-alkaloid) kappa opioid receptor agonist
- Effects are not mediated by the 5-HT(2A) receptor, the classic target of hallucinogens such as LSD
- Salvinorin A has therapeutic potential as a treatment for pain, mood and personality disorders, substance abuse and gastrointestinal disturbance (Cunningham et al., 2011)

GUESS THE DRUG

Drug A

- Competitive reuptake inhibition of serotonin, norepinephrine and dopamine
- Augments presynaptic release of serotonin, norepinephrine and dopamine
- Agonist activity at postsynaptic serotonin receptors 5-HT1 and 5-HT2 receptors
- 10 x more affinity for uptake at serotonin transporters compared to dopamine and norepinephrine transporters

Drug B

- Augments presynaptic release of serotonin, norepinephrine and dopamine
- Competitive reuptake inhibition serotonin, norepinephrine and dopamine
- 10 x more affinity for uptake at serotonin transporters compared to dopamine and norepinephrine transporters
- Agonist activity at postsynaptic serotonin receptors 5-HT1 and 5-HT2 receptors
- Agonist of the alpha-2 adrenergic receptors
- Agonist of sigma receptors
- Inhibitor of MAO A and B

Drug A

- Augments presynaptic release of serotonin, norepinephrine and dopamine
- Competitive reuptake inhibition serotonin. norepinephrine and

3,4-Methylenedioxymethamphetamine (MDMA, Ecstasy, Molly)

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receptors

Drug B

- Augments presynaptic release of serotonin, norepinephrine and dopamine
- 10 x more a Methamphetamine ared to dopamine a
- Agonist activity at postsynaptic serotonin receptors 5-HT1 and 5-HT2 receptors
- Agonist of the alpha-2 adrenergic receptors
- Agonist of sigma receptors
- Inhibitor of MAO A and B

Amphetamines

- The efficacy of low dose MDMA in the treatment of PTSD (Otalora et al., 2018) and depression (Yazar-Klosinski et al., 2017) has been recently confirmed
- MDMA, at least in the short term, may cause serotonin-mediated alterations in pain sensitivity (O'Regan et al., 2004)
- Methamphetamine is not approved for medical use but its analogue dextromethamphetamine with ten times stronger dopaminergic and, therefore, psychostimulant effect has been approved by the FDA for treating ADHD and obesity in both adults and children

Something to think about

- We can teach old dog new tricks
- DOSAGE, DOSAGE, DOSAGE
- Keep an open mind-know your pharmacology and historical context
- New legal regulative to permit clinical trials
- Bright side: we have already crossed that bridge with Cannabis