Psychedelic assisted therapy in neurological conditions

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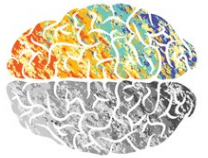
Psychedelics and pain – the early work



380

1963

Sicuteri reports moderate effects LSD 50-100 µg in the treatment of migraine

1964

50

K*ast and Collins* reports analgesic action of LSD 100 µg in patients with severe pain relating to cancer or gangrene

1967

6

Kuromaru et al report significant and sustained reduction phantom limb pain in five of six subjects receiving LSD 50 µg

128

Kast reports analgesic action of LSD 100 µg in 128 terminally ill patients. Pain reduced for 3 weeks

1969

22

Pahnke et al reports reduction in pain and depression in cancer patients treated with LSD psychotherapy

1973

31

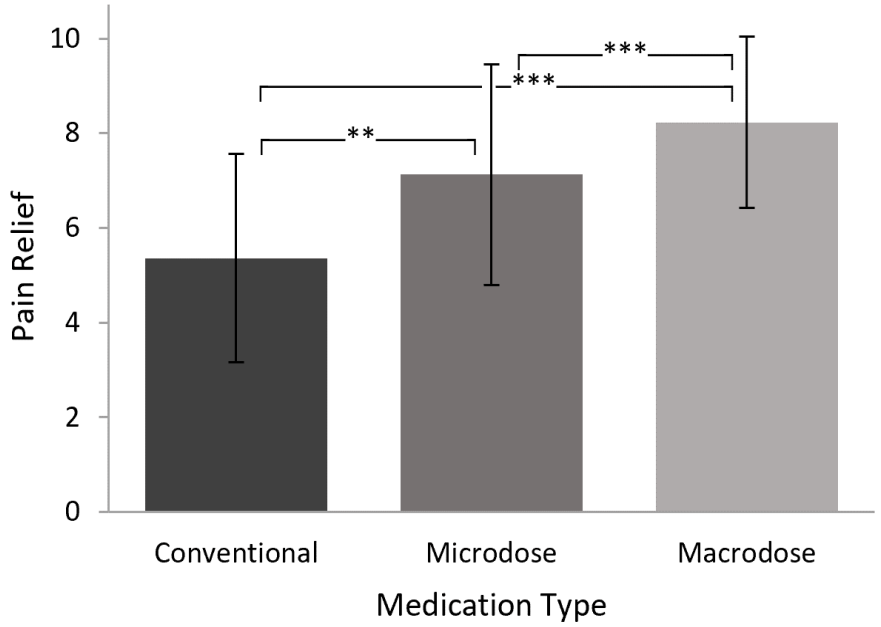
Grof et al administer LSD + psychotherapy to patients with pain, anxiety and depression and report reduction in pain severity

1977

7

Fanciullacci et al report improvement 5 out of 7 patients with phantom limb pain following repeated dosing with LSD 25-50 µg .

Psychedelics - a survey an analgesic effects among 250 chronic pain sufferers



Nature of the condition(s) : Musculoskeletal, Inflammatory, Neuropathic, Headache & orofacial, Pain caused by cancer, visceral, or other types of pain.

Rate pain intensity (0-10) after psychedelics (low or high dose) and conventional analgesics (over-the-counter pain relievers, opioids, antidepressants, anticonvulsants, cannabis or other)

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Smith et al, 2022

LSD microdosing - controlled study on analgesic effects

Maastricht University

Original Paper

A low dose of lysergic acid diethylamide decreases pain perception in healthy volunteers

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Abstract

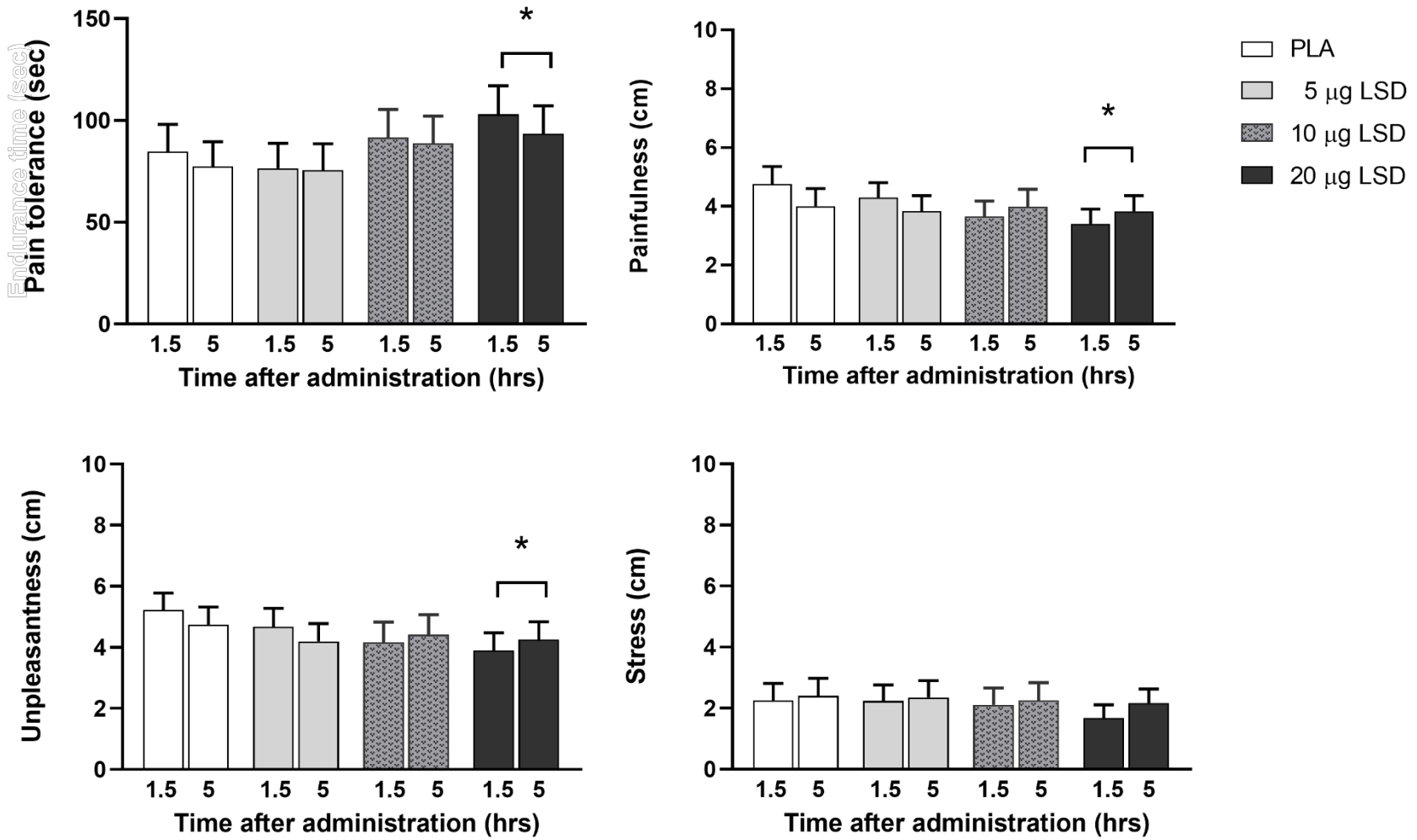
Background: Lysergic acid diethylamide (LSD) is an ergot alkaloid derivative with psychedelic properties that has been implicated in the management of persistent pain. Clinical studies in the 1960s and 1970s have demonstrated profound analgesic effects of full doses of LSD in terminally ill patients, but this line of research evaporated after LSD was scheduled worldwide.

Aim: The present clinical study is the first to revisit the potential of LSD as an analgesic, and at dose levels which are not expected to produce profound mind-altering effects.

Methods: Twenty-four healthy volunteers received single doses of 5, 10 and 20 µg LSD as well as placebo on separate occasions. A Cold Pressor Test was administered at 1.5 and 5 h after treatment administration to assess pain tolerance to experimentally evoked pain. Ratings of dissociation and psychiatric symptoms as well as assessments of vital signs were included to monitor mental status as well as safety during treatments.

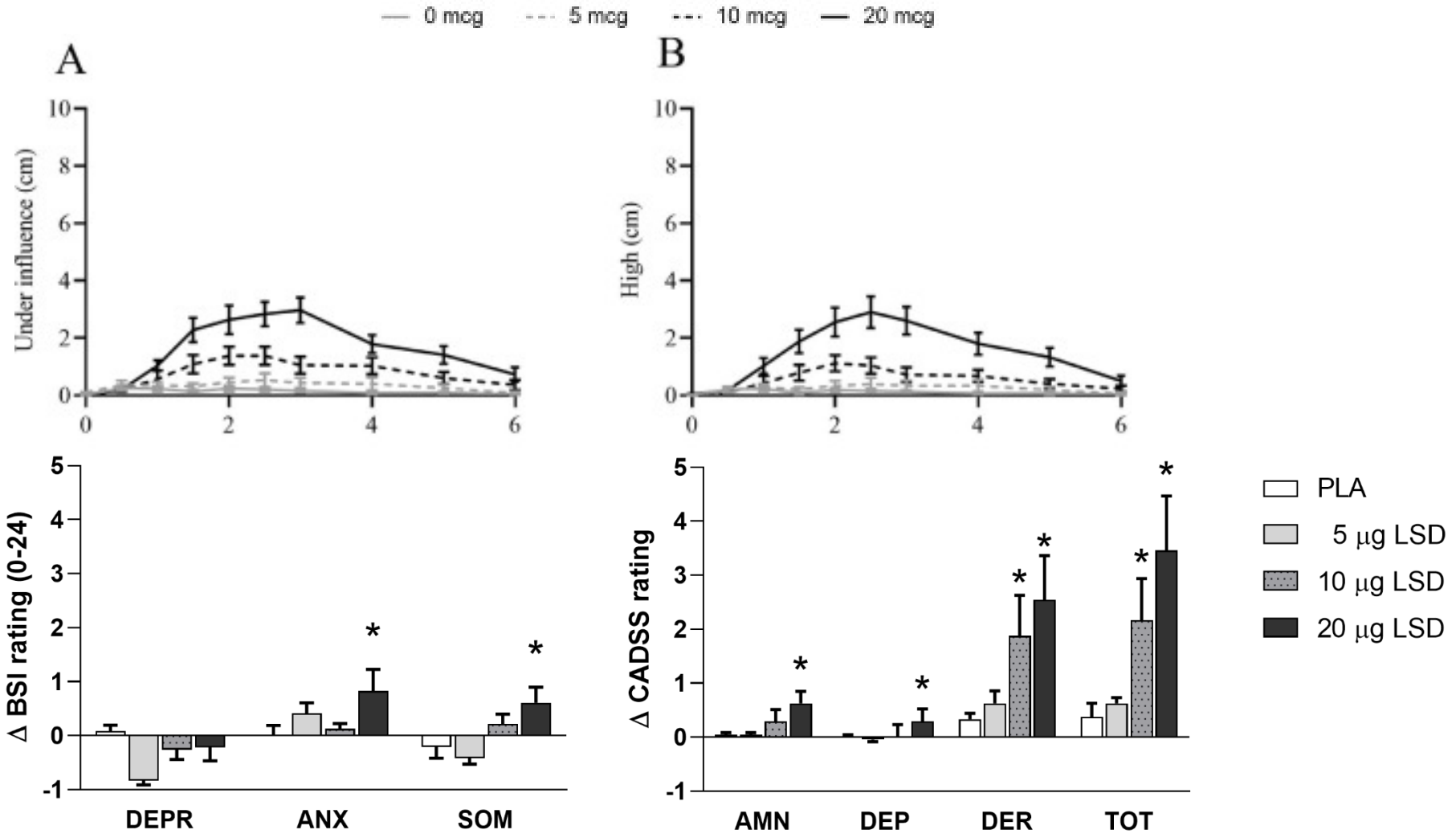
Results: LSD 20 µg significantly increased the time that participants were able to tolerate exposure to cold (3°C) water and decreased their subjective levels of experienced pain and unpleasantness. LSD elevated mean blood pressure within the normal range and slightly increased ratings of dissociation, anxiety and somatization.

LSD microdosing - analgesic effects



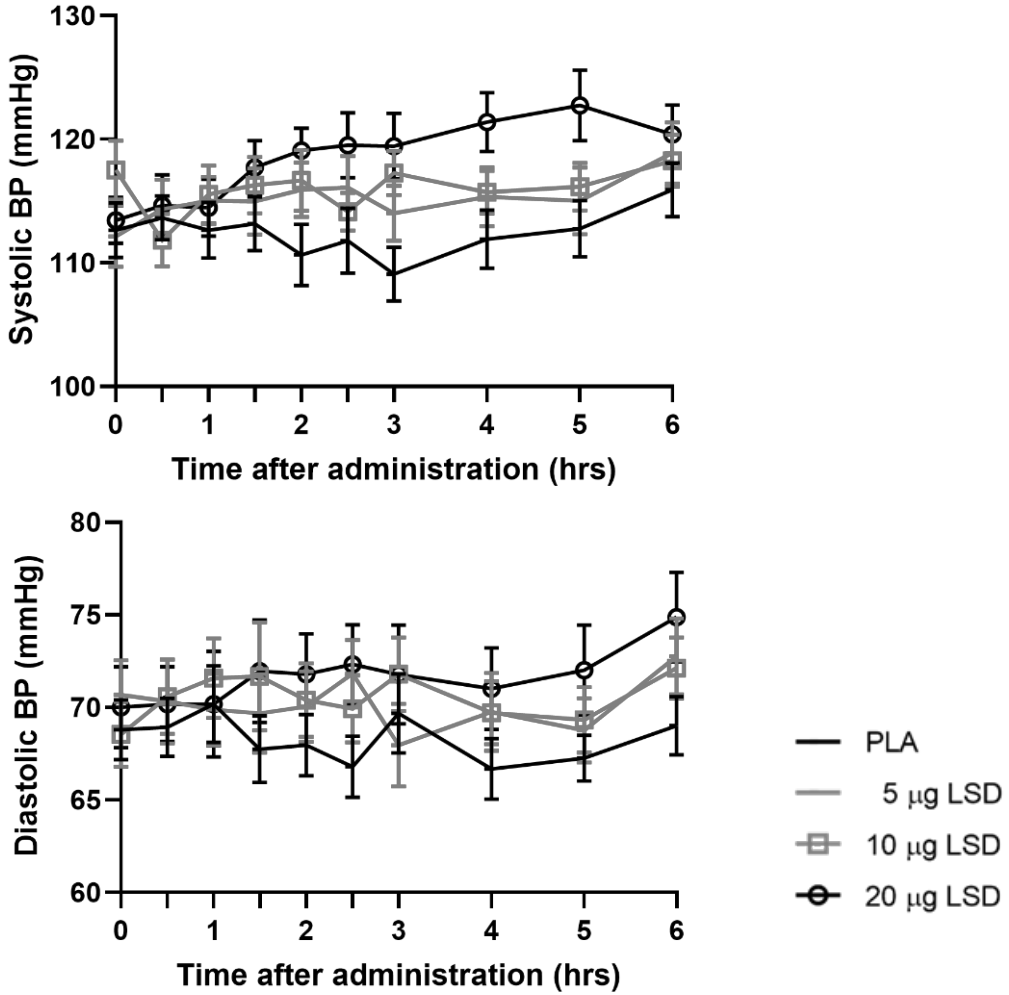
Ramaekers et al, 2020

LSD microdosing - efficacy without psychedelic effects?



Ramaekers et al, 2020; Hutten et al, 2020

LSD microdosing - mechanism of action?



- Attentional reorienting from pain sensation to the psychedelic experience of LSD

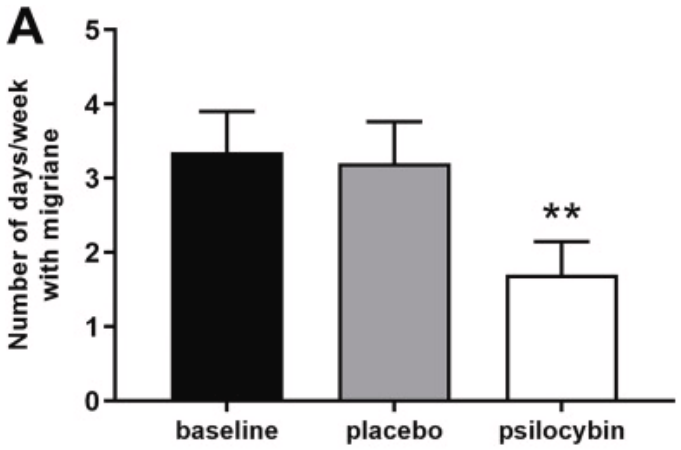
- Vasoconstrictive properties of LSD leading to elevated BP and hypoalgesia.

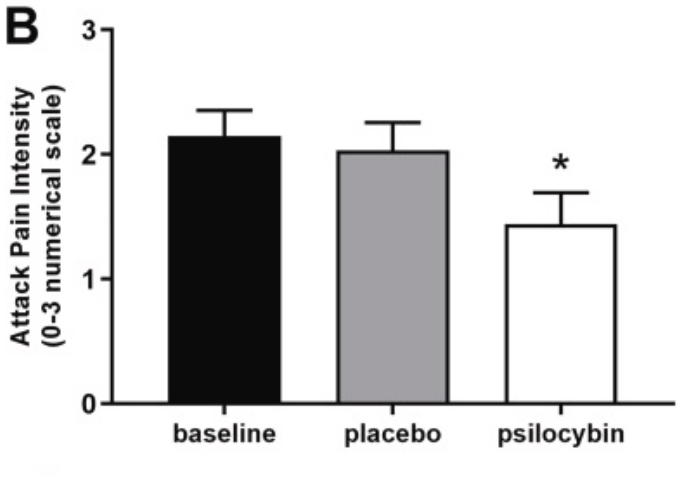
- LSD agonist of 5-HT2A and 5-HT1A receptors in the dorsal raphe, a structure known to be involved in actions of descending pain inhibitory processes

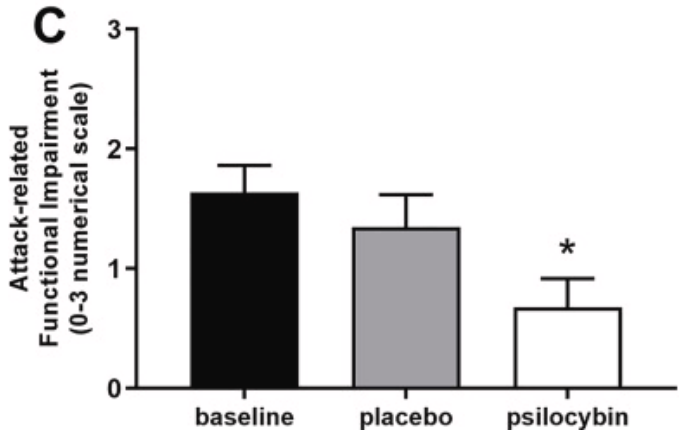
- Anti-inflammatory actions

Clinical studies with psychedelics in chronic pain patients

Patients with migraine: 2 weeks after 1 single dose of psilocybin 10mg (N=12)



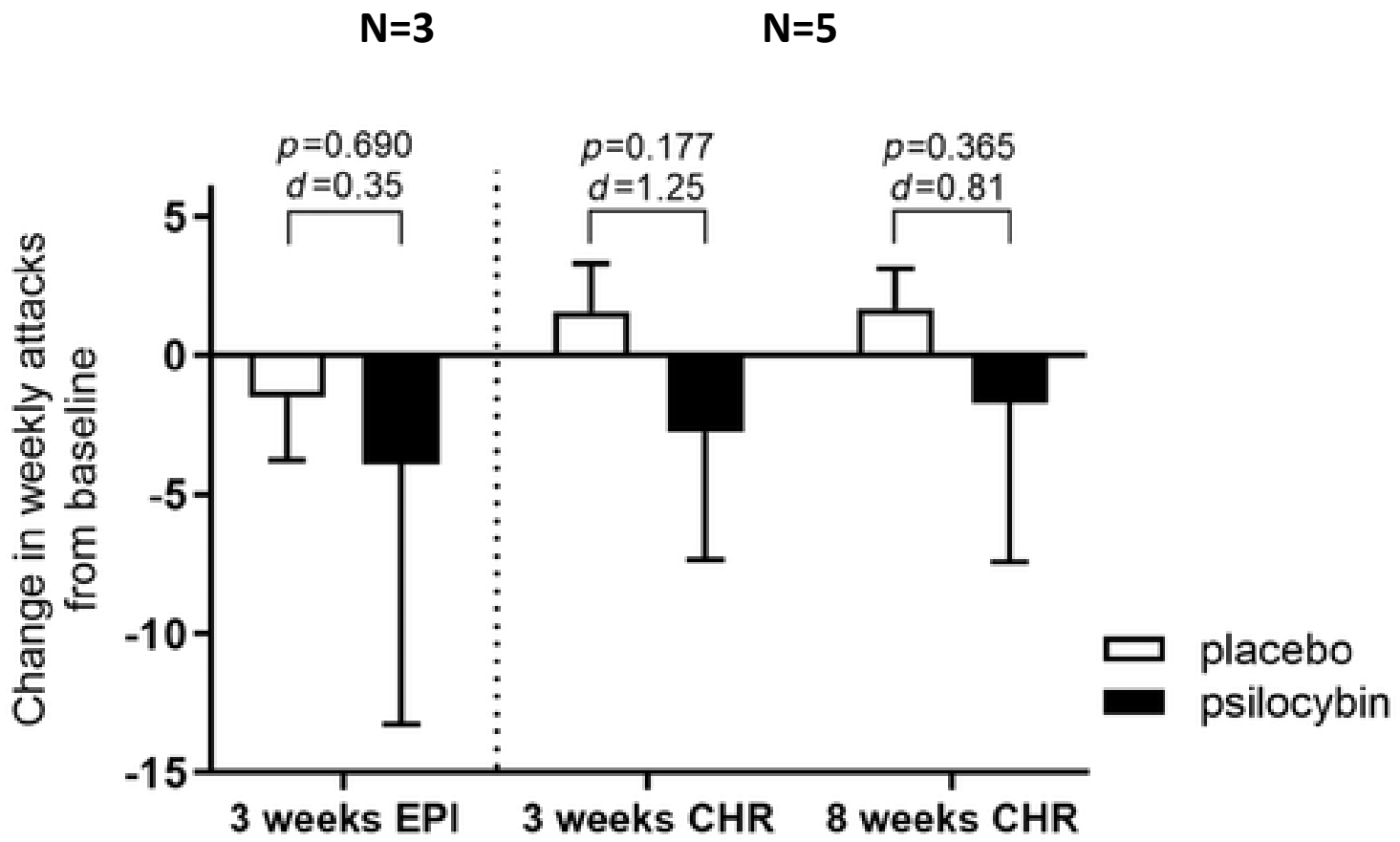




Schindler et al, 2021

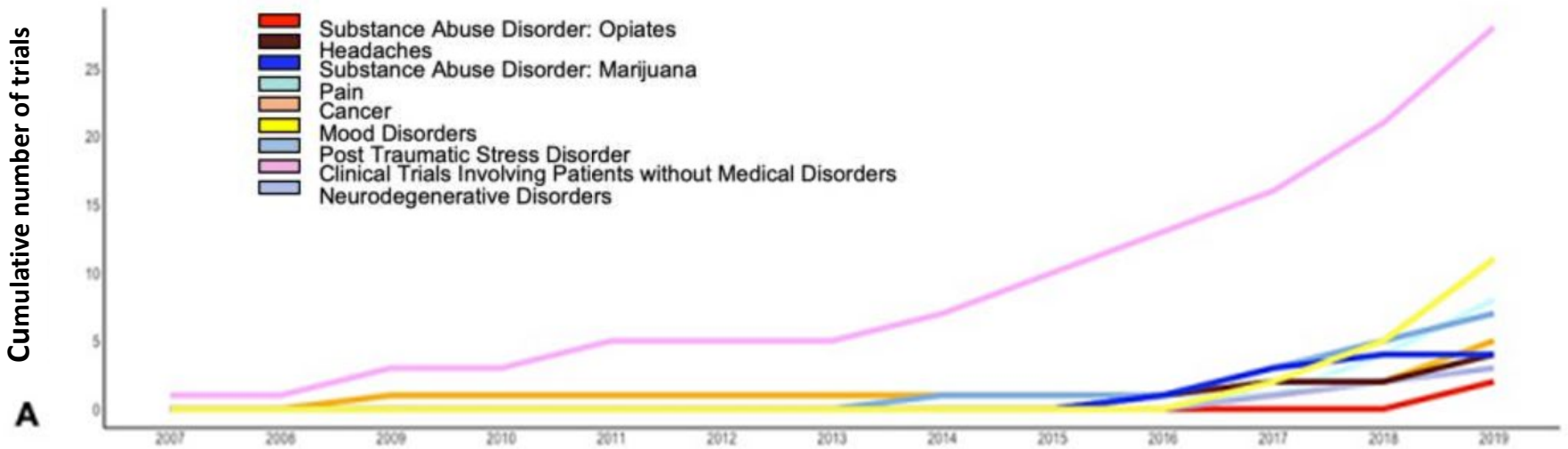
Clinical studies with psychedelics in chronic pain patients

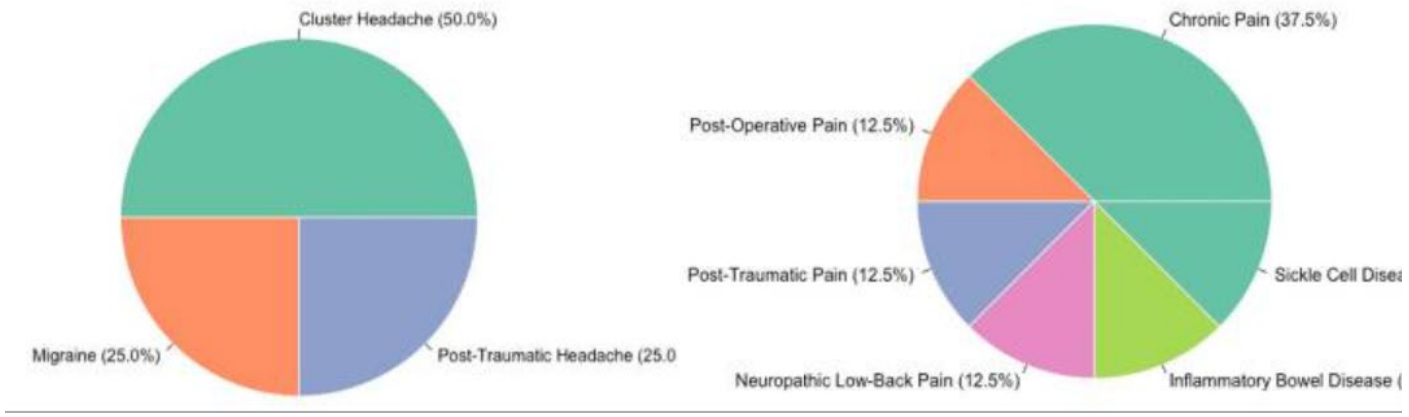
Repeated dosing with psilocybin 0.143 mg/kg (about 10mg) in patients with cluster headache



Schindler et al, 2022

Psychedelics Studies in the American Drug Trial Registry





Kurz et al, 2022

Psychedelics and pain - future challenges

- ✓Clinical trials with larger samples needed.
- ✓Tolerance? Replication at repeated doses?
- ✓Patient population, which indications?
- ✓Mechanism of action?
- ✓Clinical implementation?

Thanks!

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