

In this era of highly increasing numbers of patients with eating disorders, what new ideas and innovations would you like to bring to the field of Eating Disorders which can help our patients and their carers?

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Introduction

In an era characterised by the relentless pursuit of an idealised body image, the prevalence of eating disorders has emerged as a critical public health concern in the United Kingdom. These multifaceted and often-debilitating conditions are thought to affect up to 1.25 million people in the UK¹, with mortality rates twice as high that the general population, and with low recovery rates for illnesses like Anorexia Nervosa (AN) and Bulimia Nervosa (BN) of which 54% and ~50% respectively will never fully recover². Moreover, recent research shows that eating disorders have been significantly exacerbated by the onset of COVID-19³, thought to be caused by diminished access to healthy coping mechanisms, and diminished treatment access. However, the dynamic field of eating disorders has many new research programmes that are being established and this essay is intended to outline how pharmacologically assisted psychotherapeutic uses of psychedelics could serve as a groundbreaking innovation in patient and carer outcomes.

The most common conditions under the umbrella of eating disorders are BN, AN and Binge-Eating Disorder (BED). These conditions are distinct, but have a few shared characteristics such as a predilection towards rigid thinking⁴, emotional dysregulation⁵ & negative affectivity⁶, identity dysfunction⁷ and a sense of detachment⁴. Taking the condition of AN as an example, the ‘Vicious flower’ model of AN⁸ (Fig.1) lists some of the maintaining factors behind AN as being AN identity formation, inflexible thinking and difficulty with emotion. Different eating disorders have also been shown to be connected to other psycho-social issues, with AN linked with OCD and social issues, and BN linked with ADHD.

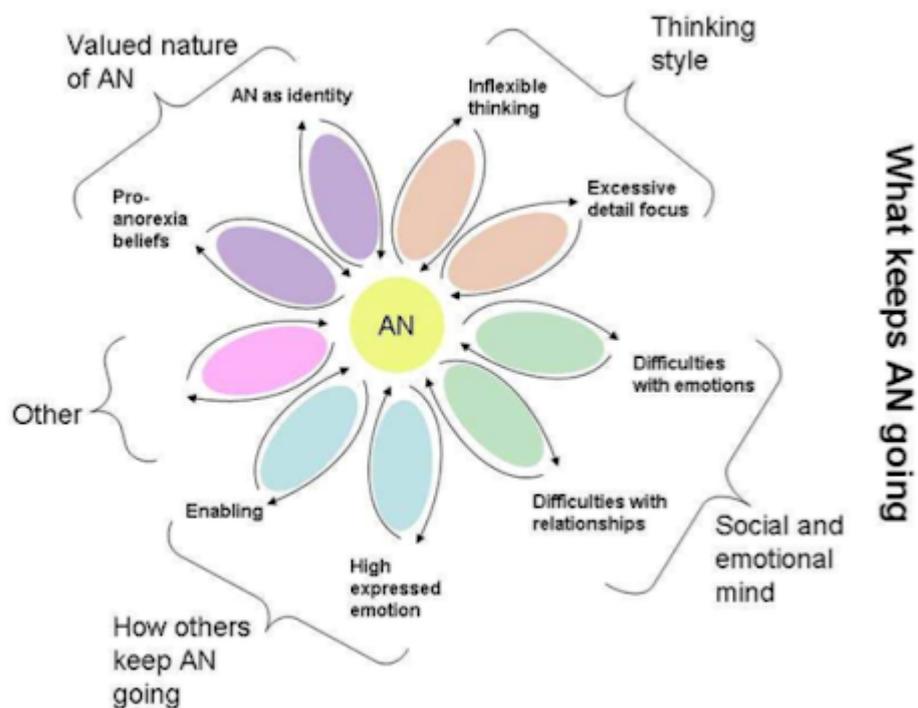


Fig.1

Psychedelics

Psychedelics such as psilocybin and lysergic acid diethylamide, are commonly used recreational drugs in the UK that are known to have profound effects on cognition, perception and emotions. Spiritual and meaningful experiences are often reported when taking these drugs,

and they have been perennially used as medications with cross-cultural origins. These drugs, however, following unethical and covert usage in the 1960s became banned substances in the 1967 UN Convention on Drugs, leading to a long-term drought of research and academic interest, hardened by socio-political attitudes by Western powers about the “war on drugs”. Despite this, psychedelics, in the modern day, present an interesting transdiagnostic therapeutic avenue, especially for the treatment of eating disorders, potentially linked to many of the aforementioned shared traits of those disorders. Brain imaging studies of individuals with AN observed 5-HT alterations, and specifically lower 5-HT_{2A} binding in parts of the frontal, parietal and occipital cortices⁹. In psychedelic drugs, the 5-HT_{2A} receptor signalling that occurs is thought to be the cause of lowered rigid thinking, and greater emotional release, inducing a positive mood and combatting detachment and emotional dysregulation, as well as increasing neuroplasticity (Fig.2). This serves in contrast to SSRIs, for example, which primarily use 5-HT_{1A} receptor signalling to decrease anxiety, but also increase emotional blunting, potentially maintaining the emotional withdrawal and sense of detachment experienced by patients. Although these both induce positive mood and wellbeing, comparing the side effect profiles, the length of treatment and the emotional blunting of SSRIs with the emotional release of psychedelics, the psychedelic drugs present a safer, and possibly more effective alternative. This is especially the case in the treatment of BN, where SSRIs are occasionally used. Furthermore psychedelic drugs have been known to cause a phenomenon named “ego-dissolution” whereby the distinction between self-representation and object representation is blurred, which is known to have profound effects on identity formation, key in the maintenance of AN. Patients with AN frequently report that their self-image is intimately intertwined with the diagnosis/state of anorexia, and their anorexic identity gives them meaning and purpose. Psychedelics may exert the pivotal force in shifting to a broader, depersonalised viewpoint from this intricately interwoven identity, which could potentially lead to the disruption of this cognitive association. In the

burgeoning psychedelic literature, this phenomenon is named “REBUS”, meaning relaxed beliefs under psychedelics

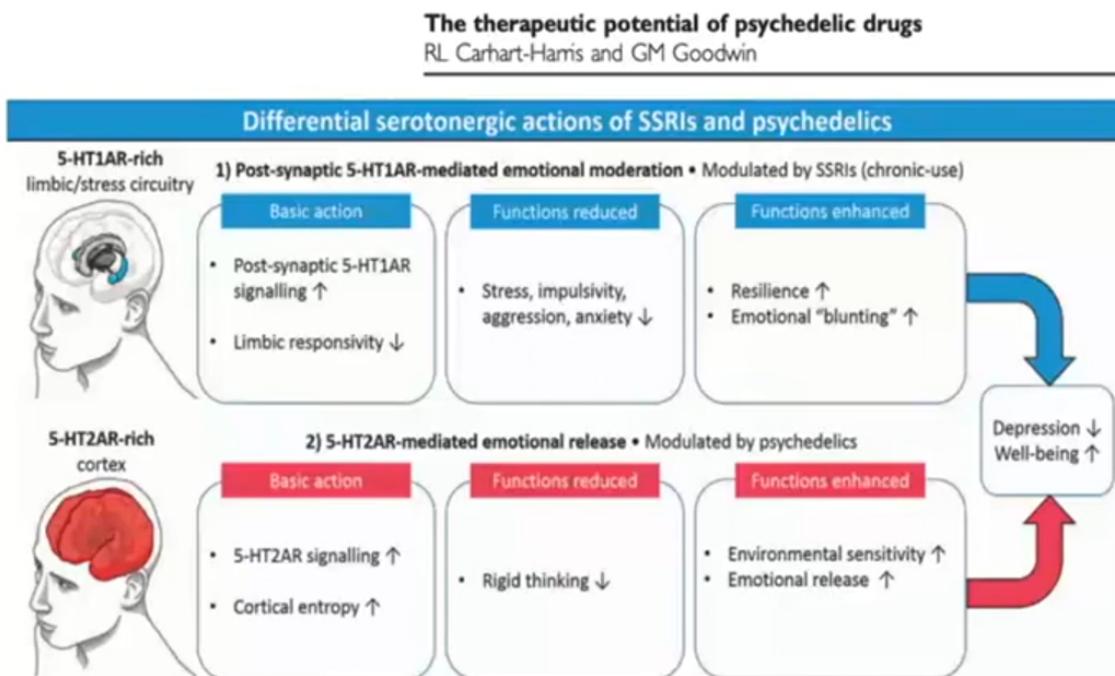


Fig.2

Psychedelics could also have an impact on carers, who routinely report emotional distance & intimacy as being among the toughest issues to manage. One carer said, “We used to have a really close relationship and now all of a sudden I can't have that relationship with her, and that really hurts. I find that very sad.”¹⁰

Psychedelics have the potential to remediate this element of the carer's relationship with their ward, through heightened emotional release which has been shown to facilitate extraversion, social openness and the fostering of social bonds. Furthermore, psychedelics could facilitate family-based therapy modalities by increasing cognitive flexibility in patients and thereby making the patient more suggestible, amenable to advice and positive encouragement.

Previous Clinical Research on Psychedelics

Preliminary data on the abuse potential of self-administration of psychedelic drugs show that the abuse liability is negligible¹¹, and therefore could present a safe alternative to current offerings, such as the high dose SSRIs occasionally used in BN management. With respect to other mental health conditions, MDMA has already shown promising results in the treatment of PTSD, with 2 doses of MDMA and psychological support found to have lasting benefits 6 months after treatment. Psilocybin has been shown in a 2021 study to be at least as effective as escitalopram in treating major depressive disorder¹² (MDD). In the two-arm double-blind placebo controlled trial one group was given a typical dose of 6 weeks daily escitalopram, and the other was given just two doses of psilocybin, with the side effect profile being significantly better in psilocybin. In an analysis of a previous 2016 study published in the Lancet, psilocybin was found to be the most efficacious single dose treatment ever¹³, which in an era of chronic antidepressant prescriptions, offers a much needed alternative. The growing evidence for transdiagnostic efficiency with conditions such as depression, anxiety, PTSD and addiction, shows promise for psychedelics' extensibility into the domain of eating disorder, especially BN and AN given their proven link with depression¹⁴. Although the specific evidence for eating disorders and psychedelics is in its infancy, the results of a recent pilot study have been published, showing 25 mg psilocybin and psychotherapy in patients with AN leading to a

significant reduction in the Eating Disorder Examination (EDE) scale from 3.5 to 0.8 after 84 days, as well as global reductions in anxiety and depression up to 84 days after¹⁵, supported by another study showing reduction in depressive symptoms, and increases in wellbeing after 2 weeks (Fig.3). Three more clinical trials on the effects of psilocybin on anorexia and binge eating disorder are ongoing, with one being completed recently.

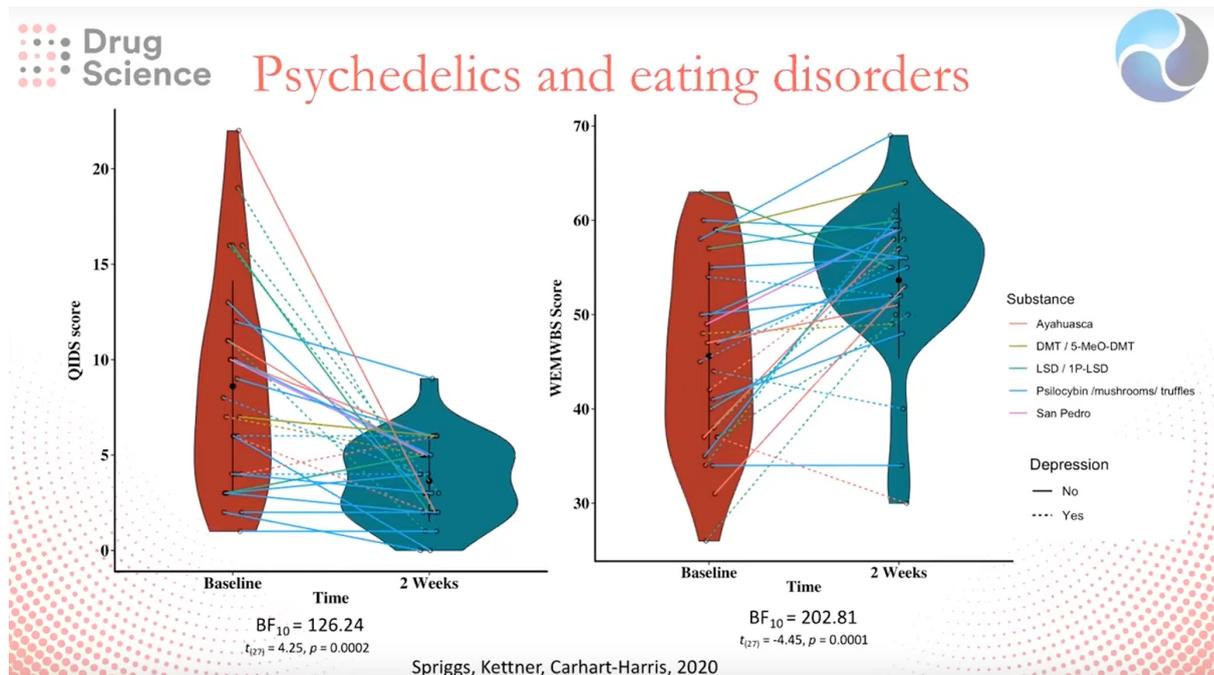


Fig.3

Logistical Factors for Widespread Uptake of Psychedelics

Practically, there are many positive factors which underscore the amenability of psychedelics to being a new paradigm-shifting innovation in the field of eating disorders. The psychedelic research cited thus far have been most published in one of two leading research centres; John Hopkins, in the USA, and Imperial College London in the UK, with both currently undertaking clinical trials on eating disorders and psychedelics. Furthermore psychedelics are becoming a hot-bed of venture investment with the reputable companies Usona and COMPASS pathways providing funding for the ongoing research. This shows that there is a level of academic and industrial interest in therapeutic pathways for psychedelics, and that funding

opportunities are available, which will facilitate new projects getting off the ground. Psychedelic assisted therapy is the name under which most psychedelic treatments are being explored, Roseman et al. comments on this that, “psychedelic therapy may be more appropriately thought of as a distinct form of (drug-assisted) psychotherapy than as a pure pharmacotherapy,” in this way, psychedelics can be seen as a bridge between pharmaco-therapeutic and psychotherapeutic treatment modalities, and foster bridge building between the two disciplines, encouraging greater future integration.

As well as this it's important to note that in contrast to the medications like antidepressants, sedatives and anti-psychotics that are used as pharmacological treatment for eating disorders, psychedelics have a ancient, cross-cultural, history of widespread use in many societies, and as such natural variants of psychedelics, should pose significantly less long-term health risks. Psychedelics have been an enduring feature of human existence across a plentitude of cultures and continents ; Siberians in Asia, Ancient Romans in Europe, the Amazonians in the Americas, as well as the Bwiti people from Gabon, Africa, to name a few¹¹. This is the inverse of the synthetically produced pharmaceuticals produced in modern times, which have not been steeped in the same history or cultural webs of meaning. It is also worth mentioning that there is invariably a stigma attached to psychedelic use stemming from the reputation of the drug's use amongst certain subcultures in the 1950s and 60s. This would need to be tackled through the government transforming their educational stance on psychedelic use, and the dissemination of teaching materials to professionals in the field of mental health. Marketing psychedelic drugs through other names such as psycho-active drugs or serotonergic hallucinogens could also be useful in uncoupling the negative connotations from these drugs.

Legal Obstacles

Caveating the immense success psychedelic drugs have found in preliminary research, they are still a Schedule 1 banned substance under the 2001 Misuse of Drugs Regulations in the UK, and as such, are notoriously difficult and expensive to acquire for clinical trials. In this aspect the UK is lagging behind other pioneers of psychedelic therapy; the US, Canada and Australia all allow pathways for psychedelics to be therapeutically prescribed, with psychedelics being on the equivalent of Schedule 2 in Australia. However, the pharmaceutical licencing body in the UK, Medicines and Healthcare products Regulatory Agency (MHRA) has sanctioned several phase II clinical trials in the last year on psychedelics and mental health disorders, and the Advisory Council on the Misuse of Drugs (ACMD) has recommended, following a letter co-signed by the Royal College of Psychiatrists themselves, to extend Schedule 2 status for research purposes to all Schedule 1 drugs¹⁶. With all this in mind, the legal viability for and the accessibility of widespread clinical trials to further test and establish the safety, efficacy and trans-diagnostic therapeutic potential of drugs seem to be on the horizon.

Conclusion

With the increasingly widespread prevalence of eating disorders, the prospect of psychedelic-assisted therapy represents a potentially ground-breaking new innovation that could reinscribe the treatment pathways of many such disorders, and lead to a paradigm shift, with cooperation between pharmaco-therapeutic and psychotherapeutic modalities. Although further legal action is needed to facilitate research and prescribing, the success of this in the near future is probable, and seems inevitable given the trajectory of other countries. The factors of safety in lack of abuse liability, transdiagnostic efficacy, one-off dosage method, plausible multi-model levels of action, institutional and venture capital funding, and empirical success in preliminary

clinical trials, all point to psychedelics being a very promising innovation in the field of eating disorders, with widespread interventions on the horizon.

Endnotes

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