ELECTIVE (SSC5a) REPORT (1200 words)

A report that addresses the above four objectives should be written below. Your Elective supervisor will assess this.

Describe the pattern of treatment-resistant depression, anxiety, and PTSD within London compared to indigenous populations in the Americas.

It is not possible to find data on London alone, instead I will look at the UK as a whole. Treatment-resistant depression (TRD) is defined as a failure of improvement in mood with the consecutive use of two different anti-depressant medications. According to the BMJ, roughly 2.7 million people in the UK, 10-30% of those with depression, suffer with TRD. The mental health charity Mind estimates that during any given week in England, 6 in 100 people will be experiencing generalized anxiety disorder, 8 in 100 mixed anxiety and depression, and 4 in 100 are affected by post-traumatic stress disorder.

The indigenous population of America, an incredibly broad term which is here used to describe those people who's ancestors were present before the colonization of what is now the US, account for about 1.5% of the US population. Nearly $1/5^{th}$ of adults from these communities suffer with mental illness, with suicide being the leading cause of death in girls between 15 to 19. Finding further data on the specific prevelance of depression, anxiety, and PTSD is difficult partly because of cultural differences in expression of mental distress but also due to an understandable mistrust in authority, and a lack of cultural sensitivity from mental health service providers to service users.

Describe the prevalence of the use/research of Psychedelic-Assisted therapy for mental illness in the UK compared to other countries around the world engaged in such research.

The first wave of psychedelic research was brutally cut down before its time due to the ever-growing War on Drugs in the 1960s. The new wave of psychedelic research, often dubbed the 'Psychedelic Renaissance', has been gently rumbling on arguably since the late 2000s but has only now started to infiltrate the mainstream. While in the UK there are still many exhausting and bureaucratic barriers to psychedelic research, mainly due to the current state of drug-policy and scheduling in this country, psychedelic research is starting to bloom. A point proven by the fact that I'm writing this as medical student at a university-approved elective taking place in an NHS-Imperial hybrid clinic dedicated soley to the development of psychedelic-based therapies.

It is difficult to describe the 'prevalence' of use/research of Psychedelic-assisted therapy due to a lack of comprehensive data. The UK, Netherlands, Switzerland, Israel and the US are among the many countries embarking on extensive psychedelic research projects. As for personal psychedelic use, places where are ancient cultural and spiritual use of psychedelics, such as in Peru, are likely to have highest prevalence of psychedelic use – particularly if the flocks of well-intentioned 'psychonauts' and gap year students are also included. The long-standing decriminlastaion of drugs in Portugal, and the more recent in Oregon and the Netherlands may also lead to a rise in psychedelic-use.

Describe the difference in psychedelic-assisted psychotherapy in London compared to 'Indigenous' use.

Psychedelic use among 'Indigenous' populations is incredibly varied and cannot be simply lumped together. Indeed, even the term psychedelic is too broad. I will therefore focus on comparing the differences between legal protocols involving psilocybin (the active ingredient in magic mushrooms) in London (and the UK more broadly) with the Mazatec people, an indigenous community in Oaxaca, Mexico. The use of psychoactive mushrooms in healing ceremonies has been happening since at least the 16th Century in Meso-America but only entered Western knowledge in the mid-twentieth century following Robert Wasson's meeting with the Mazetec people.

Perhaps the most important differences are the setting and the intent with which the psychedelics are

taken; in research centres in the UK, the setting is clinical. In the CIPPRes clinic they have beautifully set up rooms with large art installations, designed to make the environment more relaxed and reduce stress as much as possible. Nonetheless, particularly with the use of ECGs and other monitoring equipment, the process is still distinctly clinical. Usually, there will only be one other person with the patient/participant. The participant will wear an eye mask while music is played. In healthy volunteers, the intent may be to try something new or have the opportunity to explore their mind, while in patients, as it stands currently, psychedelic-assisted therapy is often done when other treatment options have run out.

During a velada, a Mazetac healing ceremony, psychoactive mushrooms (sometimes known as 'little saints') are consumed to communicate with deities or cure the spirit while guided by a Curandera (spiritual healer). The mushrooms themselves are seen as hallucinigenics or mind-expanding drugs, but channels to the divine and a part of an ancient spirituality. In these ceremonies both Curandera and participant ingest the mushroom, with prayers and chanting used to help reach the divine. This seems outward-facing journey to connect to with deities and the divine contrasts with the introspective nature of UK psychedelic-assisted therapy. Traditionally the mushrooms are consumed at night, where as this is of course not the case in the UK. There are many other differences but already those discussed raise the questions about reciprocity, appropriation and what it is we are seeking in the West when we use psychedelics.

Describe the protocols involved in psychedelic-assisted psychotherapy research and gain a basic ability to interpret the relevant brain imaging results.

Unfortunately, because there were no active studies happening while I was based at the clinic, I did not get a chance to see much brain imaging.

Thinking many different protocols in psychedelic research, varying with the type of compound being used and the intent behind its use. As with any other drugs, the different compounds have different levels of bioavailability, pharmacokinetics and pharmacokinetics. For example, a novel protocol being developed by a team at the clinic involves delivering DMT (the active ingredient in Ayahuasca) via an infusion. DMT can be smoked or ingested but has a very short half-life, giving a very intense but rapid trip. In contrast, an ayahuasca brew results in a much longer experience as compounds in the vine prevent the metabolism of the psychoactive components contained in the leaves of a separate plant. The idea is that by delivering DMT as infusion, participants can reach the expanded state of mind and then be held at a steady state at a slightly lower level. This prolonged expanded state may then allow for greater exploration of the psyche to take place.

An example of a more established protocol can be seen in the study protocol for psilocybin for anorexa nervosa (Spriggs et al., 2021). The authors have designed the study to take place over 6 weeks with 8 visits to a clinic in total and monthly data collection for the first 6 months and final follow up one year after the study is completed. Participants with anorexia nervosa are first screened for suitability, the full details of which can be seen in Table 1 of the paper. Key exclusion criteria, which are universal to studies involving psychedelic drugs are a personal and family (immediate member) history of psychosis. If participants pass the screening, there are three blocks of preparation, dosing, and integration. Preparation is what it says on the tin and gives participants a chance to voice concerns; integration similarly involves incorporating what was experienced during the dosing into each participant's mental model of themselves, their illness and the word around them. Each dose of psilocybin can be up to 25mg and a therapist and guide will be present with the participant. Questionairres, MRI,and EEG will all be used to monitor outcomes. More detail can be found in the paper by Spriggs et al. (2021), this gives an overview of the protocols used in psychedelic-assisted therapy.