

**Do autistic people attribute perceived change in mental health to a psychedelic experience?**

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**UCL Doctorate in Clinical Psychology**

**Thesis declaration form**

I confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Signature:



Name: Charlotte Rice

Date: 1<sup>st</sup> July 2022

## Overview

Over the past few years, research into psychedelic drugs has highlighted their therapeutic potential. This thesis aims to improve understanding about the therapeutic potential of psychedelics in two ways. Firstly, it aims to improve understanding of the lasting effects of psychedelics on social cognition or functioning. Secondly, it aims to improve understanding of the therapeutic potential of psychedelics in an autistic population.

This volume is comprised of three parts. Part One presents a review of literature on the lasting effects of classic psychedelic drugs on social cognition/functioning when drugs are administered by researchers. Effects on empathy, altruism, closeness and forgiveness are considered.

Part two describes an empirical study where a cross-sectional survey was used to explore autistic people's experiences of using classic psychedelics, specifically whether they attributed any perceived changes in mental health to their most impactful psychedelic experience. Factors which were hypothesised to potentially impact on psychedelic change in mental health such as 'degree of mystical experience', perceived change in psychological flexibility and perceived change in social connectedness were also considered.

Part three is a critical appraisal of the process of conducting the research described in part 2.

This was a joint project completed with Jack Stroud (Stroud, 2022).

## **Impact Statement**

The literature review and the empirical study look at different elements of the lasting effects of psychedelics. This statement will address the impacts of each in turn.

The literature review adds to the field by giving a comprehensive account of the current literature available on the lasting effects of psychedelics on social cognition and function. It both summarises the findings from the literature and assesses the quality of the evidence and is the first systematic review of these topics. The review suggests that many of the existing studies on lasting effects of psychedelics on social cognition/function are methodologically weak. So, the second benefit of the review is to suggest ways to improve future research by focusing on controlled studies with sample sizes large enough to pick up effects, using both pre and post measures and adequate doses of psychedelic drugs.

The empirical study, looking at perceived changes in mental health attributed to psychedelics in autistic population was in part inspired by autistic people (especially the Autistic Psychedelic Community) who have been sharing their experiences of using psychedelics online. This study poses potential benefits to this community by offering a quantitative study of autistic people's experiences of how psychedelics affect mental health. This research might also help wider public understanding of the reasons why members of the autistic community might use these drugs.

Taken together the review and empirical study pose potential benefits for researchers and communities outside academia who are united in an interest in the way that psychedelics could be used to address mental health problems. Although treatments for mental health problems do exist, they have variable success rates. For some people their symptoms do not improve. The development of effective, safe treatments is important for people struggling with mental health problems, which are debilitating and have both a personal and societal cost. Psychedelics, if they are administered carefully and ethically, could have a potential for use as part of treatment for mental health problems. However, before psychedelic assisted therapy can be contemplated for widespread use more research needs to be done so understanding can be increased. This thesis can add to this understanding.

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### **Part 1: Literature Review**

Do psychedelics have a lasting impact on social cognition and functioning?

## **Abstract**

### **Aims:**

This review aims to investigate the lasting effects of classic psychedelic drugs on social cognition and functioning. It reviews all studies where participants were given a classic psychedelic and a measure of social cognition/functioning was taken at least 24 hours later.

### **Methods:**

A systematic literature review was conducted using PsycINFO, Medline and Web of Science. 17 studies meeting inclusion criteria were reviewed.

### **Results:**

Controlled studies looking at empathy found mixed results with some evidence of lasting changes following psychedelic use and some showing no change. Both controlled and uncontrolled studies looking retrospectively at self-reported change in prosocial/altruistic behaviour found a lasting increase. Methodological quality of the studies was mixed with many studies lacking control groups, randomization or repeated measures.

### **Conclusions:**

Overall the literature suggests some evidence that classic psychedelics might be associated with lasting increases in empathy, prosocial behaviour, interpersonal closeness and forgiveness. However due to the low quality of the evidence available it is difficult to draw any conclusions and more evidence from randomized controlled studies using repeated measures and adequate drug doses is needed.

## **Introduction**

Social function is key to thriving in the human environment (Young, 2008). Social cognition can be defined as the mental processes through which we perceive, think about, and act toward other people (Amodio, 2018) and describes the capabilities which allow us to function in the social environment. These include capabilities such as facial/emotional perception, attribution of intent to the behaviour of others, empathy and moral reasoning (Beauchamp & Anderson, 2010). Prosocial behaviour refers to positive interactions with others, such as sharing, helping, cooperating and comforting (Hay, 1994).

Problems in social cognition are linked to poor mental health. Researchers at The Research Domain Criteria (RDoC) initiative found that social cognition was one of the key trans-diagnostic constructs critical to mental health disorders (Gur & Gur, 2016). Problems with social cognition have been found to be associated with a range of mental health conditions. A review by Kupferberg et al (2016) found that depression was associated with social impairments and poor social functioning. Empathy was found to be reduced in people with Bipolar disorder (Shamay-Tsoory et al, 2009) and major depressive disorder (Cusi et al, 2010). A meta-analysis found that people with PTSD show deficits in mentalising and emotional recognition (Plana et al, 2014) and a study showed reduced social perception/social knowledge was associated with Social Phobia (Jacobs et al, 2008). People with anxiety and mood disorders have been found to show deficits on emotional recognition tasks (e.g. Plana et al, 2014 and Pringle & Harmer, 2015) and research suggests positive effects of medication on mental health may be mediated by improvements in emotional recognition (Pringle., 2015). Autism is a neurodevelopmental condition characterised by problems with social cognition (American Psychiatric Association, 2013) and has a high co-occurrence with mental health problems (Hollocks et al, 2019). The link between Autism and anxious and depressive symptoms has been shown to be mediated by social connection (Stice & Layner, 2019).

‘Classic’ psychedelics are a class of hallucinogenic drug which act as serotonin 2A receptor (5-HT<sub>2A</sub>R) agonists (Garcia-Romeu et al, 2016) and include drugs such as lysergic acid diethylamide (LSD), psilocybin and N,N-dimethyltryptamine (DMT). Psychedelic drugs have the capacity to acutely (whilst the person is experience subjective effects) induce changes in social cognition by impacting on consciousness, perceptual processing and emotions (Roseman et al, 2019 and Kometer & Vollenweider, 2016). For example, Psilocybin has been shown to acutely produce feelings of trust, closeness to others, increased

emotional empathy and to impair recognition of sad and fearful faces (Pokorny et al, 2017) along with reducing feelings of social exclusion (Preller et al, 2016). LSD has been found to increase prosocial behaviour on the Social Value Orientation test and increased desire to be with other people (Dolder et al, 2016).

There is no consensus about what mechanisms might explain these changes, however research suggests several neuronal changes which may have the potential to explain psychedelics' effects on empathy and social functioning. Psychedelics influence the serotonin (5-hydroxytryptamine [5-HT]) system which has been shown to have a role in moral behaviour and modulate empathetic responses to others (Harmer, 2003). Second, psychedelics have been shown to decrease activity in the default mode network (Carhart-Harris et al, 2015) which has been hypothesised to reduced self-focus and increase capacity to focus on others (Speth et al, 2016). Thirdly, psychedelics are linked to increased bilateral insular activity. For example, Cabanis et al (2013) found non self-serving bias correlated with increase bilateral insular activity.

To date there have been no reviews looking at whether the acute effects of psychedelics on social cognition and social function persist in the longer term. Long term effects on social cognition and functioning may have valuable clinical implications. A better understanding of these long-term effects would contribute to debates about whether psychedelics are promising candidates for treating mental health problems and might suggest what type of problems they are suited to addressing. If psychedelics do have lasting effects on social cognition this may also provide clues to the potential mechanisms of change for psychedelic assisted therapy.

Psychedelics have been shown to be an effective treatment for mental health problems such as depression (Carhart-Harris et al, 2016), anxiety (Gasser et al, 2014) and alcohol misuse (Bogenschutz et al, 2018) with improvements lasting after acute effects have worn off. A qualitative study looking into the mechanisms by which psychedelic assisted psychotherapy helped participants with treatment-resistant depression found consistent themes of increased connections to others (Watts et al, 2017).

This review sets out to systematically search for and review studies on post-acute effects of classic psychedelics on social cognition or prosocial behaviour and asks:

1. Do psychedelics have long term effects on social cognition or social functioning?
2. Which areas of social cognition/functioning do psychedelics effect?

## Method

### Search Strategy

A systematic search was conducted using databases PsycINFO, Medline and Web of Science between January 1994 and December 2021 (see table 1 for search terms). 1994 was selected as the start of modern psychedelic research when Strassman et al.'s (1994) study became the first to administer classic psychedelics after several decades of prohibition in the USA. Table 1.1 shows the search terms used.

**Table 1.1**

*Summary of search terms*

Category	Type of Term	Terms Used
<b>Drug terms</b>	General Terms	<ul style="list-style-type: none"> <li>▪ Psychedelic* or hallucinogen* or entheogen*</li> <li>▪ 5-HT2AR agoni* or 5HT2AR agoni* or serotonin 2A receptor agoni* or 5-hydroxytryptamine 2A receptor</li> </ul>
	Specific Terms	<ul style="list-style-type: none"> <li>▪ Lysergic acid diethylamide or LSD-25 or LSD 25 or lysergide</li> <li>▪ Psilocybin or O-phosphoryl-4-hydroxy-N,N-dimethyltryptamine or psilocin or 4-PO-psilocin or 4-PO-HO-DMT</li> <li>▪ Mescaline or 3,4,5-trimethoxyphenethylamine or peyote</li> <li>▪ N,N-Dimethyltryptamine or Dimethyltryptamine or N,N-DMT</li> <li>▪ Bufotenin* or 5-HO-DMT</li> <li>▪ 5-MeO-DMT or 5-methoxy-N,N-dimethyltryptamine or O-methylbufotenine*</li> <li>▪ ayahuasca or yage</li> </ul>
	Subject Heading Search	<ul style="list-style-type: none"> <li>▪ PsycINFO: exp hallucinogenic drugs</li> <li>▪ Medline: exp hallucinogens</li> <li>▪ Web of Science: No subject headings</li> </ul>
<b>Social Terms</b>	General Terms	<ul style="list-style-type: none"> <li>▪ Social* or socio-emotional or socioemotional or emotion* or interpersonal*</li> </ul>
	Specific Terms	<ul style="list-style-type: none"> <li>▪ Empath*</li> <li>▪ Face or facial</li> </ul>

	<ul style="list-style-type: none"> <li>▪ Attribution</li> <li>▪ Moral*</li> <li>▪ Generosity</li> <li>▪ Communicat*</li> <li>▪ Mentaliz*</li> </ul>
Subject	▪ PsycINFO: Exp social perception or exp social cognition
Heading	▪ Medline: Exp social perception or exp social cognition
Search	▪ Web of Science: No subject headings

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### **Inclusion/Exclusion criteria**

The inclusion criteria are as follows:

1. Study must involve the use of a ‘classic psychedelic’. Classic psychedelics are hallucinogenic drugs which act as serotonin 2A receptor (5-HT<sub>2A</sub>R) agonists (Garcia-Romeu et al., 2016) and include drugs such as ayahuasca, LSD, psilocybin. This does not include hallucinogens which have different mechanisms of action such as MDMA, Ketamine or cannabis.
2. Study must include a measure of social cognition and/or social functioning (e.g. empathy, emotional recognition, prosocial behaviour). This could include self-report or task-based measures.
3. For a study to be included it must fulfil one of two requirements. Firstly, experimental studies with either a between subjects (e.g. testing drug vs placebo) or repeated measures (comparing pre drug with post drug measures) design. This would include studies that fulfil these requirements completed in naturalistic settings. Secondly follow ups of these studies are also included where measures look at long term social effects (e.g. the Persisting Effects Questionnaire (PEQ)) by asking about retrospective change.

The exclusion criteria are as follows:

1. Studies that look at acute effects only. This review is interested in effects that persist beyond the acute period where participants are actively under the influence of the

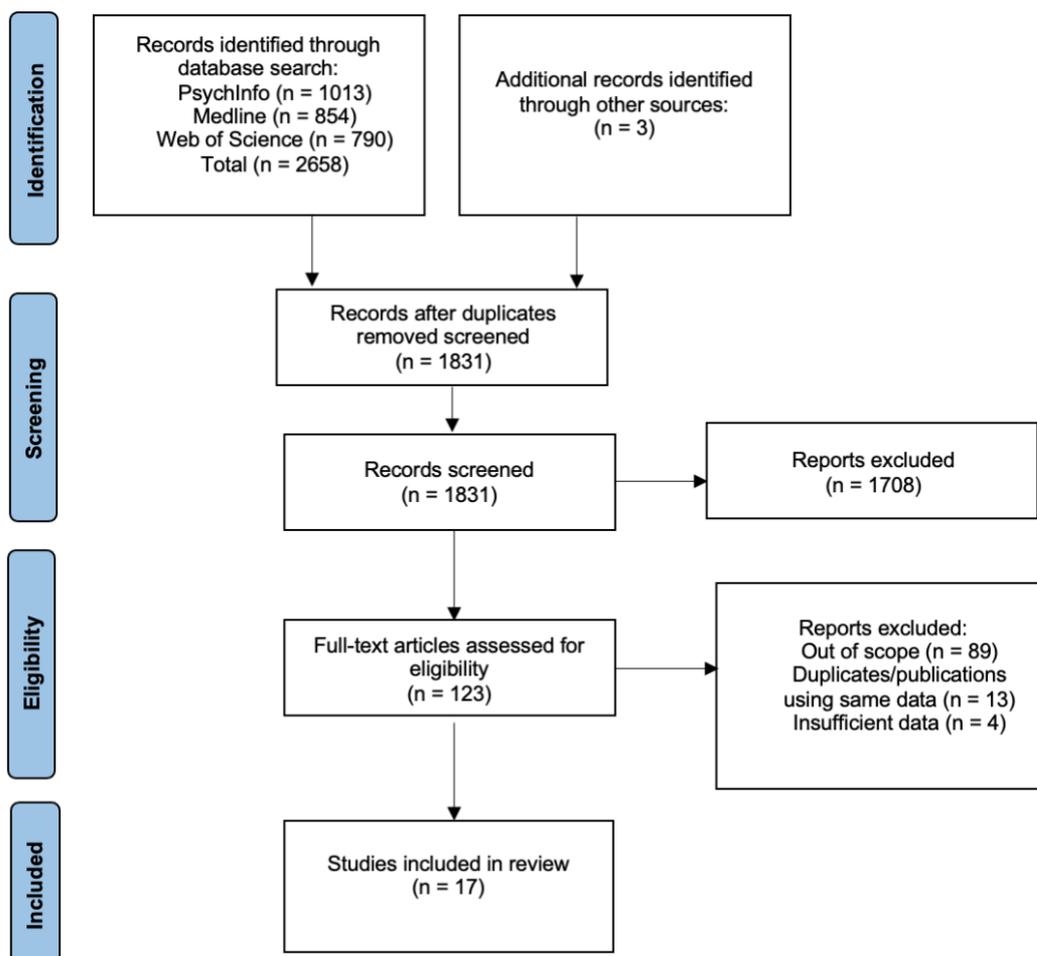
drug and the user is experiencing noticeable effects. Studies which only measure within the first 24 hours will be excluded. This timescale comes from a controlled study found that participants reported almost all noticeable subjective effects of LSD and psilocybin lasted less than 24 hours (Holze et al., 2022).

2. Studies where the administration of the drug was not overseen by an experimenter. (i.e. studies where participants self-report having taken a drug but there is no way to accurately know what drug and what dose were administered).
3. Studies looking at animals.
4. Studies using small/micro doses.

### Study Selection Process

**Figure 1.1**

*Diagram explaining the flow of papers through the screening process*



## **Summary/coding procedures**

After being selected for review studies were split into three categories for analysis; studies looking at prosocial behaviour/altruism (n=8) are described in tables 1.6 and 1.7, studies looking at empathy/emotional recognition (n=8) are described in tables 1.4 and 1.5 and studies looking at other areas of social cognition/functioning (n=4) are described in table 1.8. Two studies (Kiraga et al., 2021 and Griffiths et al., 2018) appear in two categories as they looked at multiple outcome variables.

## **Appraising methodological Quality of the studies**

JBI critical appraisal tools (Joanna Briggs Institute, 2020) were used to critique and appraise the research evidence. Two different tools were used depending on the design of the study: the checklist for randomized controlled trials (for studies which included randomisation) the checklist for quasi-experimental studies (for studies with either did not use randomisation). Table 1.6 summarises the appraisal of the studies.

A second reviewer was utilised at three stages of the study. They screened 10% (183) of papers identified through the database search for eligibility. They extracted data from 22.5% (4) of the studies and assessed 29% for methodological bias. At the screening stage both reviewers had a 98.91% level of agreement, at the extraction stage there was a 100% level of agreement and at the assessment of bias stage there was an 89.47% level of agreement.

## Results

### Overview of studies

Most studies used psilocybin (11) or ayahuasca (5) with one using LSD, all drugs were given orally in either a capsule or as a liquid. The studies approached placebos differently. In studies which used placebos, five used other drugs which would mimic some of the effects of psychedelics. For example Agin-Liebe et al (2020) and Ross et al (2016) used Niacin which produces a tingling sensation similar to psilocybin. Four others used a capsule with an inert substance such as lactose and two used a very low dose (1mg) of psilocybin.

Follow up times ranged from 1 day after taking the psychedelic to 4.5 years after with the mean follow up time being around 6 months.

Sample sizes in the studies tended to be quite low with the median sample size of 19 participants completing each study.

Five studies used clinical populations, with two of these looking at the same group of participants with treatment resistant depression (Roseman et al., 2018 and Stroud et al., 2018), two looking at the same group of participants with anxiety related to cancer (Agin-Liebe et al., 2020 and Ross et al., 2016) and one looking at people with social anxiety (Dos Santos et al., 2021). The other twelve studies looked at 'healthy' participants who reported no psychiatric diagnosis.

### Study Design and Methodological Quality

There was a lot of variation in the methodology used by the studies and therefore the quality of the evidence was mixed. Some studies used randomized control groups, some used control groups with no randomization, some used repeated measures with no control group and some followed up participants to take a retrospective measure of change. Table 1.2 presents a summary of the designs. Figure 1.2 presents a key for deciphering which of five different designs is used throughout the review. Table 1.3a and 1.3b presents findings from JBI critical appraisal tools. Studies with more than one design are included twice.

**Table 1.2***Summary of designs of studies included*

First Author/year	Measure	Control Group	Randomisation	Repeated Measures	Follow up
Agin-Liebe et al (2020)	WHOQOL-BREF	X	X	X	●
Barrett (2018)	Emotional discrimination STROOP	X	X	●	X
Dos Santos et al (2021)	Recognition of Emotions in Facial Expressions (REFE)	●	●	●	X
Griffiths et al (2006)	Persistent Effects Questionnaire (PEQ)	●	●	X	●
Griffiths et al (2008)	Persistent Effects Questionnaire (PEQ)	X	X	X	●
Griffiths (2011) A	Persistent Effects Questionnaire (PEQ) A	●	●	●	X
	Persistent Effects Questionnaire (PEQ) B	X	X	X	●
Griffiths et al (2018)	Trait Forgiveness Scale, (TRIM- 18)	●	●	●	X
	Interpersonal closeness (IOS)	●	●	●	X
	Persistent Effects Questionnaire (PEQ)	●	●	X	●
Johnson et al (2017)	Persistent Effects Questionnaire (PEQ)	X	X	X	●
Kiraga et al (2021)	Multifaceted empathy test (MET)	X	X	●	X
	Persistent Effects Questionnaire (PEQ)	X	X	X	●
Madsen et al (2020)	Persistent Effects Questionnaire (PEQ)	X	X	X	●
Mason et al (2019)	Multifaceted empathy test (MET)	X	X	●	X
Rocha et al (2021)	Recognition of Emotions in Facial Expressions (REFE)	●	●	●	X

Roseman et al (2018)	BOLD fMRI emotional faces images task	X	X	●	X
Ross et al (2016)	Persistent Effects Questionnaire (PEQ)	X	X	X	●
Schmid et al (2018)	Persistent Effects Questionnaire (PEQ)	X	X	X	●
Smigielski et al (2019)	Life changes Inventory (LCI-R) 'concern for others' section	●	●	●	X
Stroud et al (2018)	Dynamic Emotional Expression Recognition Task (DEER-T)	X	●	●	X
Uthaug et al (2021)	Multifaceted empathy test (MET)	●	●	●	X

● = study includes  
 X = study does not include

### Figure 1.2

#### Key explaining study designs

Study Design	Code
Randomised Control design with repeated measures	
Randomised Control design (no repeated measures)	
Control Group (no randomisation) with repeated measures	
Repeated measures (no control group)	
Follow up using retrospective measures (no control group or repeated measures)	

**Table 1.3a**

*Analysis of Randomised Control Studies using JBI critical appraisal tool*

First Author/year	Was true randomization used for assignment of participants to treatment groups?	Was allocation to treatment groups concealed?	Were treatment groups similar at the baseline?	Were participants blind to treatment assignment?	Were those delivering treatment blind to treatment assignment?	Were outcomes assessors blind to treatment assignment?	Were treatment groups treated identically other than the intervention of interest?	Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analysed?	Were participants analysed in the groups to which they were randomized?	Were outcomes measured in the same way for treatment groups?	Were outcomes measured in a reliable way?	Was appropriate statistical analysis used?	Was the trial design appropriate, and any deviations from the standard RCT design (individual randomization, parallel groups)
Dos Santos et al (2021)	●	●	●	●	●	●	●	●	●	●	●	●	●
Griffiths et al (2006)	●	●	●	●	●	●	●	●	●	●	●	●	●
Griffiths et al (2011a)	●	●	●	●	●	●	●	●	●	●	●	●	●
Griffiths et al (2018)	●	●	●	●	●	●	●	●	●	●	●	●	●
Rocha et al (2021)	●	●	●	●	●	●	●	●	●	●	●	●	●
Smigielski et al (2019)	●	●	●	●	●	●	●	●	●	●	●	●	●
Uthang et al (2021)	●	●	●	●	●	●	●	●	●	●	●	●	●

- = Yes
- = Unclear
- = No
- = NA

**Table 1.3b**

*Analysis of Non Randomised Control Studies using JBI critical appraisal tool*

First Author/year	Is it clear in the study what is the cause and what is the effect (i.e. there is no confusion about which variable comes first)?	Were the participants included in any comparisons similar?	Were the participants included in any comparisons receiving similar treatment, other than the exposure or intervention of interest?	Was there a control group?	Were there multiple measurements of the outcome both pre and post the intervention/exposure?	Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analysed?	Were the outcomes of participants included in any comparisons measured in the same way?	Were outcomes measured in a reliable way?	Was appropriate statistical analysis used?
Agin-Liebe et al (2020)	Green	Grey	Grey	Red	Red	Green	Grey	Green	Green
Barrett et al (2018)	Green	Grey	Grey	Red	Green	Green	Grey	Green	Green
Griffiths et al (2008)	Green	Grey	Grey	Red	Red	Green	Grey	Green	Green
Griffiths et al (2011b)	Green	Grey	Grey	Red	Red	Green	Grey	Green	Grey
Johnson et al (2017)	Green	Grey	Grey	Red	Red	Green	Grey	Green	Grey
Kiraga et al (2021)	Green	Grey	Grey	Red	Red	Red	Grey	Green	Green
Madsen et al (2020)	Green	Grey	Grey	Red	Red	Green	Grey	Green	Green
Mason et al (2019)	Green	Grey	Grey	Red	Red	Red	Grey	Green	Green
Roseman et al (2018)	Green	Grey	Grey	Red	Red	Green	Grey	Green	Green
Ross et al (2016)	Green	Grey	Grey	Red	Red	Green	Grey	Green	Green
Schmid et al (2018)	Green	Grey	Grey	Red	Red	Yellow	Grey	Green	Green
Stroud et al (2018)	Green	Red	Green	Green	Red	Green	Green	Green	Green

- = Yes
- = Unclear
- = No
- = NA

## **Empathy and Emotional Recognition**

Empathy can be defined as the ability to vicariously experience and/or understand the affect of others (Lockwood, 2016). Empathy can be broken down into two components: emotional and cognitive empathy. Emotional empathy relates to how someone feels in response to someone else's emotional state; whether they can feel what the other feels. Cognitive empathy is about being able understand how another person feels without being in the same affective state, for example being able to accurately recognise emotions in other people.

### **Studies using the Multifaceted Empathy Task (MET)**

The Multifaceted Empathy Task (MET) (Dziobek et al, 2008) measures both emotional and cognitive empathy. Participants are asked to rate concern and arousal they feel in response to emotional images (to measure emotional empathy) and are asked to correctly identify the mental state of the person in the image (to measure cognitive empathy). Studies looking at acute effects of psychedelics found an increase in emotional empathy and decrease in cognitive empathy. One study looking at the acute effects of psilocybin on the MET showed it increases emotional empathy but not cognitive empathy 160 minutes after ingestion (Pokorny et al, 2017) and a study looking at the acute effects of LSD also found increased emotional empathy but a reduction in cognitive empathy five and seven hours after ingestion (Dolder et al, 2016).

**Table 1.4***Summary of results of studies using the MET*

	<b>Mason 2019</b>		<b>Kiraga 2021</b>		<b>Uthang 2021</b>
					
<b>Type of Empathy</b>	<b>1 day</b>	<b>1 week</b>	<b>1 day</b>	<b>1 week</b>	<b>1 day</b>
<b>Cognitive Empathy (CE)</b>					
Total	×	×	↑	↑	-
Positive Faces	×	×	↑	↑	-
Negative Faces	×	×	↑	×	-
<b>Emotional Empathy (Implicit) (EEI)</b>					
Total	↑	-	×	↑	-
Positive Faces	↑	×	×	↑	×
Negative Faces	↑	↑	×	×	↑
<b>Emotional Empathy (Explicit) (EEE)</b>					
Total	↑	×	×	×	-
Positive Faces	×	×	×	×	×
Negative Faces	↑	×	×	×	×

↑ = significant increase in relation to baseline  $P < 0.05$ 

× = no significant changes

- = no data

Three studies (Mason et al, 2019, Kiraga et al, 2021 and Uthaug et al, 2021) used the MET to look at the post-acute effects of ayahuasca on empathy. They measured empathy one day (Uthaug et al, 2021) or one day and one week (Mason et al, 2019 and Kiraga et al, 2021) after ayahuasca was ingested in naturalistic, ceremony type settings. Kiraga et al (2021) found that relative to baseline there were increases in cognitive empathy (CE) (recognition of emotions) after the ayahuasca ceremony. This was the first study to show an increase in cognitive empathy measures on the MET post psychedelics. It contrasts with Mason et al (2019) and Uthaug et al's (2021) findings which show no change in CE and with studies looking at acute effects of psychedelics which found impairments in cognitive empathy (e.g. Kometer, 2012, Dolder et al, 2016).

All three studies found increases in Implicit Emotional Empathy (IEE). Kiraga et al (2021) found increases in participants ratings of IEE towards positive emotions one week but

not one day after the ceremony. Mason et al (2019) found increases in IEE for both positive and negative emotions the day after the ceremony with increases in reaction to negative emotions persisting until seven days after use. Uthang et al (2021) found increases in IEE one day after the ceremony in response to negative faces only. Table 1.4 presents a summary of studies using the MET.

### Studies using Emotional Recognition Tasks

Emotional recognition tasks measure cognitive empathy, the ability to understand how another person feels without being in the same affective state. Tasks such as the Recognition of Emotions in Facial Expressions task (REFE) (Ekman et al., 1976) and the Dynamic Emotional Expression Recognition Task (DEER-T) (Platt et al., 2010) measure the sensitivity and/or accuracy with which participants are able to determine emotional states from images of emotional faces.

A review looking at the acute effects of LSD or psilocybin on emotional recognition found that LSD and psilocybin reduced the recognition of negative emotions in most studies (Rocha et al 2019). Table 1.5 summarises studies measuring post-acute emotional recognition.

**Table 1.5**

*Summary of studies looking at emotional recognition*

First Author + date	Drug + dose	Sample	Measure	Design	Follow up	Findings
Barrett, 2008	Psilocybin 25ml/kg	12	fMRI		1 week  1 month	↓ BOLD response to emotional faces in left and right amygdala.  × BOLD response to emotional faces in left and right amygdala returned to baseline.

Barrett, 2008	Psilocybin 25ml/kg	12	Emotional Recognition Task Emotional Discrimination Task Emotional Conflict Stroop		1 week	<ul style="list-style-type: none"> <li>× No changes in accuracy of facial emotional recognition</li> <li>↑ Performance accuracy on Emotional Discrimination task</li> <li>× No changes in Emotional Conflict Stroop</li> </ul>
					1 month	<ul style="list-style-type: none"> <li>× No changes in accuracy of facial emotional recognition</li> <li>↑ Performance accuracy on Emotional Discrimination task</li> <li>× No changes in Emotional Conflict Stroop</li> </ul>
Dos Santos 2021	Ayahuasca 2ml/kg	17	Recognition of Emotions in Facial Expressions (REFE)		7 days	<ul style="list-style-type: none"> <li>↑ Accuracy in ayahuasca group</li> <li>↓ Reaction time in ayahuasca group</li> <li>× No time x group interaction</li> </ul>
					14 days	<ul style="list-style-type: none"> <li>↑ Accuracy in ayahuasca group</li> <li>↓ Reaction time in ayahuasca group</li> <li>× No time x group interaction</li> </ul>
					21 days	<ul style="list-style-type: none"> <li>↑ Accuracy in ayahuasca group</li> <li>↓ Reaction time in ayahuasca group</li> <li>× No time x group interaction</li> </ul>
Rocha 2021	Ayahuasca 1ml/kg	21	Recognition of Emotions in Facial		1 day	<ul style="list-style-type: none"> <li>× No time x group interaction</li> </ul>

		Expressions (REFE)				
					7 days	× No time x group interaction
					14 days	× No time x group interaction
					21 days	× No time x group interaction
					3 months	× No time x group interaction
Roseman 2018	Psilocybin 10mg (safety dose) + 25mg	19	BOLD fMRI emotional faces images task		1 day	↑ BOLD response to negative emotional faces in the right amygdala  × No change in BOLD response to other emotional faces
Stroud 2018	Psilocybin 10mg (safety dose) + 25mg	17	Dynamic Emotional Expression Recognition Task (DEER-T)		1 week	↑ Speed of emotional recognition in psilocybin group  ↔ Interaction between group and timepoint

↑ = Significant increase in relation to baseline  $P < 0.05$

↓ = Significant decrease in relation to baseline  $P < 0.05$

× = No change

↔ = Significant interaction between time and group  $P < 0.05$

BOLD = Blood oxygenation level dependent (BOLD) imaging in fMRI

Two studies (Dos Santos et al, 2019 and Rocha et al, 2021) used the REFE task to compare emotional recognition before and after ayahuasca use in a naturalistic setting (ayahuasca ceremony) using control groups who also took part in the ceremonies after taking a placebo drug. Dos Santos (2019) compared baseline REFE scores of 14 participants (7 who received a drug and 7 who received a placebo) with score 7 days, 14 day and 21 days after ayahuasca use. They found a general significant effect of time in the ayahuasca group for both accuracy and reaction time with accuracy increasing and reaction time decreasing as

more time went by. However they found no significant time x group interaction between the ayahuasca and placebo suggesting no evidence for the effect of the drug. In the ayahuasca group only there was a significant reduction in reaction time for faces of fear, disgust and anger and an increase in accuracy for sad faces but again there was no time x group interactions.

A similar, randomized placebo-controlled trial with 21 participants (12 in the control group and 11 in the ayahuasca group) by Rocha et al (2021) had similar findings. Compared with placebo ayahuasca did not modify the REFE - there was no significant time x group interaction between ayahuasca and placebo. Again, they found a significant effect of time on accuracy in general with accuracy tending to increase over time and a significant effect on reaction time in general, but, unlike the Dos Santos (2019) study, this effect was not only found in the ayahuasca group.

Stroud et al (2018) used the Dynamic Emotional Expression Recognition Task (DEER-T) (described in detail by Platt et al., 2010) to measure emotional recognition in participants with treatment resistant depression. They compared reaction times before and 1 week after either taking psilocybin or a placebo control. They found evidence for a group x time interaction on speed of emotional recognition. At baseline the patients in the drug group were slower than the healthy control group whereas after psilocybin there was no difference. In the psilocybin group emotional recognition was faster at 1 week follow up than baseline whereas in the control group there was no difference. Change in reaction time in patients was also correlated with clinical improvement.

Barrett et al (2008) compared pre drug baseline to 1 week and 1 months after psilocybin was administered in a hospital setting on three tasks. They used an emotional recognition task, an emotional discrimination stroop and an emotional conflict stroop. Unlike the three previously mentioned studies Barrett et al (2008) found no effect of time point on accuracy of emotional recognition with near ceiling scores on all conditions. They did however find that performance accuracy on an emotional discrimination task increased from baseline to 1 week and 1 month. No effect of time was observed on the emotional conflict stroop task. This study did not use a control group so it is difficult to know if changes observed on the emotional stroop were likely due to order effects.

## **Studies looking at response to emotional faces in fMRI**

FMRI scans have been used in two studies (Barrett et al, 2008 and Roseman et al, 2018) to look for observable changes in how the brain processes emotional faces after taking psilocybin. Blood oxygenation level dependent (BOLD) imaging was used to generate images showing regional differences in cerebral blood flow which delineates regional activity.

The amygdala has been shown to be highly responsive to emotional stimuli such as emotional faces (Hariri et al, 2002). fMRI studies looking at acute effects of psilocybin found reduced amygdala activity and connectivity when viewing negative emotional facial expressions (Kraehenmann et al, 2015 and Grimm et al, 2018). A review by Rocha et al (2019) found psychedelic drugs modulated amygdala activity and that this was correlated with anti-depressant effects.

Barrett et al (2008) looked at amygdala responses to negative emotional stimuli. They found a significant reduction in BOLD response to all emotional faces in the left and right amygdala one week after taking psilocybin compared to baseline. However, both left and right amygdala response returned to baseline levels after one month.

Roseman et al, 2018 found the opposite. Using the same group of participants as Stroud et al, 2018 (people with treatment resistant depression), Roseman et al, 2018 used fMRI to look at amygdala response to neutral, fearful and happy faces. They compared baseline measures taken one week before psilocybin to measures taken one day after and found there was a significant increase in BOLD response to fearful faces in the right amygdala and these changes were predictive of clinical improvements. No significant differences were found between responses to neutral or happy faces and no differences were found in the left amygdala.

## **Altruism/Prosocial behaviour**

Prosocial behaviour, conceptualised as the antithesis of the more familiar construct of antisocial behaviour, refers to behaviour designed to benefit others, such as sharing, helping, cooperating and comforting (Hay, 1994). Studies looking into acute effects of psychedelics (the effects observed less than 24 hours after taking the drug) on altruistic behaviour found psychedelics can increase measures of altruism. LSD increased altruistic behaviour as measured using the Social Value Orientation Test (SVO) five and seven hours after ingestion (Dolder et al, 2016) and psilocybin reduced punishment in ultimatum games in male participants 1 hours after ingestion (Gabay et al, 2019).

### **Studies using the Persisting Effects Questionnaire**

The Persisting Effects Questionnaire (PEQ) (Griffiths et al, 2006) was designed to measure changes in attitudes, behaviour, spiritual experiences, and mood after the acute phase of psychedelic use. It is an 89-item self-report questionnaire which asks people to retrospectively rate changes following psychedelic use. It contains 8 items designed to measure altruism and positive social effect and 8 reversed items measuring antisocial and negative social effects, all scored on a six-point scale. It asks questions about sensitivity to the needs of others, service to others, tolerance of others, positive relationships, love for others, interpersonal sensitivity, expression of anger and social concern. Scores are expressed as a percentage of the maximum possible score.

From the literature review there were nine studies which reported using the PEQ to follow up participants after experimental psychedelic use. These studies were either placebo controlled (for example they compared the PEQ between participants who had taken the drug or participants who had taken a placebo) or were follow ups from studies with no control group where all participants had taken drug. Table 1.6 summarises studies with no control group and table 1.7 summarises results from studies with a control group.

**Table 1.6**

*Summary of non-experimental studies where the PEQ is measured ordered by length of follow up*

<b>Follow up length</b>	<b>First Author + date</b>	<b>Drug + Dose</b>	<b>Sample Size</b>	<b>Design</b>	<b>Altruistic/positive social effects Mean (SEm if reported)</b>	<b>Antisocial/negative social effects</b>
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1 week	Kiraga et al. 2021	Ayahuasca DMT 57.44mg (SD = 25.77)	17		33 (3.12)	11.35 (0.78)
2 weeks	Ross et al. 2016 (1)	Psilocybin 0.3mg/kg	14		49.58 (2.76)	0.84 (0.69)
1 month	Griffith et al. 2011	Psilocybin 20mg	18		52.0 (5.9)	1.2 (0.9)
1 month	Griffith et al. 2011	Psilocybin 30mg	18		54.6 (5.7)	0.8 (0.9)
1 month	Schmid et al. 2018 (1)	LSD 200 µg	14		23.2 (5.9)	1.0 (0.9)
7-8 weeks	Griffiths et al. 2006 (1)	Psilocybin 30mg/70kg	36		46.6 (5.5)	0.7 (0.5)
3-4 months	Madsen et al. 2020	Psilocybin 0.2mg/kg or 0.3mg/kg	10		16	0.67
6 months	Griffiths et al. 2018	Psilocybin 30mg/70kg	18		53.24 (5.85)	0.36 (0.36)
26 weeks	Ross et al. 2016 (group 1)	Psilocybin 0.3mg/kg	11		52.49 (2.98)	0.71 (0.72)
26 weeks	Ross et al. 2016 (group 2)	Psilocybin 0.3mg/kg	12		53.36 (2.86)	3.27 (0.69)
12 months	Johnson et al. 2017	Psilocybin 20mg/70kg	15		57.6 (6.2)	6.5 (2.6)
12 months	Schmid et al. 2018 (2)	LSD 200 µg	14		28.4 (6.3)	1.8 (1)
14 months	Griffiths et al. 2011 (2)	Psilocybin 20mg + 30mg	18		54.1 (6.5)	2.5 (0.9)
14 – 16 months	Griffiths et al 2008 (2)	Psilocybin 30mg/70kg	36		46.3 (5.4)	0.6 (0.4)

Nine uncontrolled studies reported scores from the altruistic/positive social effects subscale of the PEQ from participants that had taken psychedelics. These studies measured the PEQ between one week and 16 months after the drug was taken (table 1.6 shows each time point a measure was taken including studies taking more than one measurement at different times). Where multiple drug groups were included in the paper (Griffiths, 2011 and Ross et al, 2016) these are shown separately. Seven studies followed up participants who took psilocybin, one looked at ayahuasca and the other LSD.

For the altruistic/positive social effects mean scores on the PEQ ranged from 16 (Madsen et al, 2020) to 57.6. The average across all studies and timepoints was 45.48 (all scores are expressed as a percentage of the maximum possible score). For antisocial/negative social effect scores ranged from 0.36 (Griffiths, 2018) to 11.35 (Kiraga et al, 2021), with the average across all studies and timepoints as 2.11.

For psilocybin the mean PEQ score of altruistic/positive social effects across 206 participants from six studies (with 11 time points) was 49.18. For LSD across 28 participants from one study (with two time points) the PEQ score was 25.8 and for ayahuasca across 17 participants from one study the score was 33. For psilocybin the mean PEQ score for the antisocial/negative social effects across 206 participants from six studies (with 11 time points) was 1.44. For LSD across 28 participants from one study (with two time points) the score was 1.4 and for ayahuasca across 17 participants from one study the score was 11.35.

Across all drugs and timepoints the altruistic/positive social effects are much larger than the antisocial/negative social effects. There appear to be some differences between different drugs with participants who have used LSD and ayahuasca rating less altruistic/positive social changes than participants who took psilocybin.

**Table 1.7**

*Summary of studies using PEQ as part of a placebo controlled design*

<b>Follow up length</b>	<b>First Author + date</b>	<b>Drug + Dose</b>	<b>Design</b>	<b>Findings</b>
2 weeks	Ross et al. 2016 (timepoint 1)	Psilocybin 0.3mg/kg Placebo: Niacin		<p>↑** Significant increase in Altruism/positive social effects from psilocybin compared with placebo.</p> <p>× No difference in antisocial/negative social effects between psilocybin and placebo.</p>
1 month	Griffiths et al. 2011	Psilocybin 0mg/70kg + 5mg/70kg + 10mg/70kg +		<p>↑* Significant increase in Altruism/positive social effects between from 5mg/70kg, compared with 0mg psilocybin.</p>

		20mg/70kg + 30mg/70kg		<p>↑* Significant increase in Altruism/positive social effects between from 10mg/70kg, compared with 0mg psilocybin.</p> <p>↑* Significant increase in Altruism/positive social effects between from 20mg/70kg, compared with 0mg psilocybin. Also significant increase compared with 5mg/70mg and 10mg/70mg.</p> <p>↑* Significant increase in Altruism/positive social effects between from 30mg/70kg, compared with 0mg psilocybin. Also significant increase compared with 5mg/70mg and 10mg/70mg.</p> <p>× No difference in antisocial/negative social effects between any psilocybin or non psilocybin conditions.</p>
7-8 weeks	Griffiths et al. 2006	<p>Psilocybin 30mg/70kg</p> <p>Placebo: Methylphenidate hydrochloride (40mg/70kg)</p>		<p>↑*** Significant increase in Altruism/positive social effects from psilocybin compared with placebo.</p> <p>× No difference in antisocial/negative social effects between psilocybin and placebo.</p>
4 months	Griffiths et al. 2018	<p>Psilocybin 30mg/70kg</p> <p>Placebo: Very low dose psilocybin (1mg/70kg)</p>		<p>↑*** Significant increase in Altruism/positive social effects from psilocybin compared with placebo.</p> <p>↑*** Significant increase in Altruism/positive social effects from psilocybin + social support compared with placebo.</p>

				× No difference in antisocial/negative social effects between psilocybin and placebo.
				× No difference in antisocial/negative social effects between psilocybin + social support and placebo.
6 months	Ross et al. 2016 (timepoint 2)	Psilocybin 0.3mg/kg Placebo: Niacin		↑*** Significant increase in Altruism/positive social effects from psilocybin (in both psilocybin groups compared with placebo).
				× No difference in antisocial/negative social effects between psilocybin and placebo.

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↑ = Significant increase compared to placebo

\* =  $p < 0.05$

\*\* =  $p < 0.01$

\*\*\* =  $p < 0.001$

Three studies (Ross et al, 2016, Griffiths et al 2006, and Griffiths et al, 2018) used parallel control groups to compare long term effects of psychedelics to placebos. Significant differences in the PEQ Altruism/positive social effects subscale between psilocybin and placebo control groups were found in all three studies at follow up. No long-term differences between psilocybin and controls were found for the antisocial/negative social effects.

One study looked at the effects of either increasing or decreasing doses of psilocybin (Griffiths et al, 2011) and measured PEQ scores one month afterwards. They found that compared to baseline (no psilocybin capsule) the same participants who took 5mg/70kg, 10mg/70kg, 20mg/70kg or 30mg/70kg scored significantly higher on the PEQ Altruism/positive social effects subscale one month later. Participants also scored significantly higher after taking 20mg/70kg and 30mg/kg than after taking 5mg/70kg and 10mg/70kg. This suggests that long term changes are dose dependent. Again, no long-term differences were found for the antisocial/negative social effects.

## Studies measuring concern for others

Concern for others can be measured by a sub-scale on the Life Changes Inventory (LCI-R), a self-report measure that includes items looking at desire to help others, compassion for others and tolerance of others (Greyson & Ring, 2004). The scale was originally designed to be used in the context of near-death experiences and was adapted by the authors to look at retrospective change following psychedelic use. No studies have directly looked at acute changes in concern for others. Table 1.8 summarises the findings from a study on post-acute effects of psychedelics on concern for others.

**Table 1.8**

*Summary of other studies looking at Altruism/Prosocial Behaviour*

First Author + date	Drug + dose	Follow up length	Measure	Design	Findings
Smigielski 2019	Psilocybin 0.315kg/kg	4 months	Concern for others  Life changes Inventory (LCI-R) 'concern for others' section  Self rated and rated by closely related person		↑* - Concern for others in psilocybin group compared to placebo group at 4 month follow up on self report LCI-R.  × - no significant differences between psilocybin and placebo group at follow up on observer LCI-R ratings

\* =  $p < 0.05$

Smigielski et al, (2019) was the only study that looked at the long term impact of psychedelics on concern for others. They found that self-reported concern for others was significantly increased four months after taking psilocybin compared to the placebo group. Observer ratings (ratings from someone close to the participant of any changes they had observed) showed no significant differences.

## Other studies looking at other aspects of social functioning

Two studies looked at other aspects of social functioning, specifically quality of social relationships, interpersonal closeness and forgiveness. Research into acute effects of

psychedelics found that very recent psychedelic use (within the past 24 hours) predicted feelings of connectedness as measured by the inclusion of other in the self scale (IOS) (Forstmann et al, 2020). No studies have looked at acute effects of psychedelics on forgiveness. Table 1.9 summarises the results of studies looking at post acute changes in social connection, relationships and forgiveness.

**Table 1.9**

*Summary of studies looking at other measures of social cognition/functioning*

First Author + date	Drug + dose	Follow up length	Measure	Design	Findings
Agin-Liebe 2020	Psilocybin 0.3mg/kg	6 months	Social Relationships		× - no significant changes between baseline and follow up
		3.2 years	WHOQOL-BREF Social Relationships		× - no significant changes between baseline and follow up
		4.5 years	WHOQOL-BREF Social Relationships		× - no significant changes between baseline and follow up
Griffiths 2018	Psilocybin 20mg/70kg + 30mg/70kg	7 months	WHOQOL-BREF Forgiveness		× - no significant differences between psilocybin group compared to baseline
			Trait Forgiveness Scale		× - no significant differences between psilocybin and placebo group at follow up
		7 months	Forgiveness		↑* Benevolence motivation in psilocybin group compared to baseline
			TRIM-18 Benevolence motivation Avoidance motivation		↓* Avoidance motivation in psilocybin group compared to baseline
	7 months	Interpersonal Closeness		↑* IOS in psilocybin group compared to baseline	

Inclusion of the other in the self (IOS)

× - no significant differences between psilocybin and placebo group at follow up

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\* =  $p < 0.05$

\*\* =  $p < 0.01$

\*\*\* =  $p < 0.001$

## Relationships

Agin-Liebe (2020) looked at quality of social relationships 0.6, 3.2 and 4.5 years after participants with life threatening cancer received psilocybin alongside preparatory and post drug psychotherapy sessions. They used the social relationships section of the WHOQOL-BREF (a quality of life assessment tool, World Health Organization, 1994) to measure self-reported quality of relationships. This measure uses a likert scale asking participants to rate three domains - personal relationships, social support and sex life - to make a composite score. They did not find any significant differences between baseline and any of the three follow ups.

## Closeness to others

Griffiths et al (2018) used the Inclusion of the Other in the self scale (IOS) (Aron et al, 1992) as a measure of interpersonal closeness 7 months after Psilocybin or a placebo.

They found that the psilocybin group reported more interpersonal closeness at the 7 month follow up than at baseline. However there was no significant difference between the placebo and the psilocybin group. For a third group of participants (who received psilocybin plus extra support) there was a significant increase in interpersonal closeness reported compared to the placebo group. This suggests the extra support (receiving 35 hours of support around meditation, spirituality and journaling) on top of psilocybin or the interaction between support and psilocybin that improved feelings of interpersonal closeness.

## Forgiveness

Griffiths (2018) also looked at changes in forgiveness. They compared participants who had taken psilocybin to participants who took a placebo at baseline and 6 months after taking the drug/placebo. They looked at two measures of forgiveness, the *Trait Forgiveness Scale*, a measure of trait forgiveness (Berry et al, 2005) and the *TRIM-18*, a scale assessing

forgiveness of interpersonal transgression (McCullough et al, 1998). They planned to look at a third scale (the 3-item *Forgiveness* subscale of the Brief Multidimensional Measure of Religiousness/Spirituality *BMMRS* (The Fetzer Institute, 1999)) but removed it from the analysis due to groups scores being significantly different at baseline.

On the trait forgiveness scale, which measures the disposition to forgive interpersonal transgressions over time and across situations (Berry et al, 2005) they found no change from baseline in either psilocybin or placebo group and no differences between the groups at follow up.

On the TRIM-18, which has subscales measuring benevolence motivation (having goodwill for people who transgress) and avoidance motivation (the desire to avoid a transgressor) significant differences were found between baseline and 6 month follow up and between the psilocybin and placebo group. Benevolence motivation increased at 6 month follow up in psilocybin but not in the placebo group. Avoidance motivation on the other hand decreased at 6 month follow up in the psilocybin group but not in the placebo group.

## **Discussion**

This paper systematically reviewed literature on post-acute social effects of psychedelics on participants who were given psychedelics as part of an experiment. It looked at effects on altruism/prosocial behaviour, empathy, emotional recognition, forgiveness, relationships and feelings of connection with others.

### **Studies looking at Empathy**

Three studies looked at the post acute effects of empathy as measured by the MET. Results were varied with only one study (Kiraga et al, 2021) finding improvements in cognitive empathy and only one study finding an increase in explicit emotional empathy (Mason et al, 2019). All three studies (Kiraga et al, 2021, Mason et al, 2019 and Uthang et al, 2021) found increases in implicit emotional empathy. However, the studies differed on whether these changes were in response to positive or emotional faces.

The three studies differed in their methodology with Kiraga et al (2021) and Mason et al (2019) both using a repeated measures design without a parallel control group. This method does not control for practice effects which may explain why participant scores improved on the cognitive empathy emotional recognition task. Changes in empathy could also result from non-variables, for example the social or spiritual experience. Uthaug et al (2021) used a repeated measure between participants allowing them to control for practice effects or other confounders relating to the experience. They found an increase in only emotional empathy to negative stimuli compared to placebo.

These three studies were all conducted in naturalistic settings, measuring empathy in volunteers before and after they used ayahuasca as part of a retreat. The studies were conducted across Europe, mainly in the Netherlands but also in Spain and Germany. Naturalistic studies have some benefits, the studies have high ecological validity and findings may have more relevance to real world psychedelic users.

Another limitation of the uncontrolled Kiraga et al (2021) and Mason et al (2019) studies was that drop-out rates, especially for the second follow up one week after the ceremony. This high drop out rate might have biased the results.

In all three studies a large part of the sample had used psychedelics previously. This could pose a problem when trying to isolate long term effects because participants may have experienced changes from previous psychedelic use that make current changes less likely – for example changes from psychedelic use may not be summative or have a ceiling effect. The baseline measures help as they compare changes only in the time period since the current drug use.

Four studies (Dos Santos et al, 2019, Rocha et al, 2021, Stroud et al, 2018 and Barrett et al, 2008) looked exclusively at measures of cognitive empathy, looking at the effect of psilocybin or ayahuasca on performance in emotional recognition tasks compared to controls. Results were mixed. Dos Santos et al (2019) found an effect of time, with those in the ayahuasca group reacting more accurately and quicker than at baseline. They found no effect of time in the control group. Rocha et al (2021) also found an effect of time but for both the ayahuasca group and placebo group. Neither found a time x group interaction. Lack of time x group interactions suggest changes over time could be due to factors other than drug such as learning effects or effects from other aspects of the ceremony. The fact that effects were only seen in the ayahuasca group for the Dos Santos (2019) study could suggest an increase in sensitivity to negative facial emotions which may be picked up in a study with a bigger sample size and higher power. This fits with Findings from Kiraga et al's (2021) uncontrolled study which found an increase in cognitive empathy one and seven days after ayahuasca.

The authors suggest several reasons for the lack of findings. Firstly that the dose (2mg/kg and 1mg/kg) could be too low, studies looking at acute effects on REFE found that effects were dose dependent and increased as the dose went up (Dolder, 2016 & Bershad, 2019). In the Rocha et al (2021) study there was a main effect of time for both ayahuasca and placebo groups suggesting possible learning effects. Due to the small sample size and high levels of educational attainment within the participants it is also possible that high performance levels of all participants could lead to ceiling effects making it difficult to identify changes. Unlike the other three studies, Barrett et al (2008) found no effect of time point on accuracy of emotional recognition similarly finding near ceiling scores on all conditions in an uncontrolled study. Stroud et al (2018) found a significant interaction supporting the idea that effects are not due to learning effects, unlike Dos Santos et al (2019), Rocha et al (2021) and Barrett et al (2008). However, in this study there was no randomization between the drug and control group. In the drug group participants had a diagnosis of

treatment resistant depression and scored lower on the cognitive empathy measure at baseline compared to the non-clinical sample in the control group. It could be that psilocybin's post-acute effects on emotional recognition are more pronounced in people who struggle with emotional recognition for example people experiencing depression (Plana et al., 2014 & Pringle & Harmer., 2015). If more evidence confirmed this to be the case this could suggest a useful clinical implication for people with Depression.

Two studies using fMRI found contradicting results, Barrett et al (2008) found a post-drug reduction in BOLD response to emotional faces in amygdala whereas Roseman et al (2018) found an increased BOLD response to fearful faces. Barrett et al's (2008) results fit with findings from acute studies which showed reduced amygdala activity when viewing negative emotional facial expressions (Kraehenmann et al, 2015 and Grimm et al, 2018). The increase in response to fearful faces found by Roseman et al (2018) contrasts with research into SSRIs which have been shown to cause lasting decreases in amygdala response to negative emotional stimuli, which has been hypothesised to be a mechanism of anti-depressant action (Ma et al, 2015). This finding suggests that potential mechanisms of anti-depressant action in psychedelics could be different from the effect of classic anti-depressants. Both these studies are uncontrolled and have small sample sizes making it hard to draw any real conclusions.

Overall it is difficult to draw any firm conclusions about these studies. Controlled studies with non-clinical samples mainly found no lasting effects on empathy with one finding an increase in implicit empathy in response to negative emotions (Uthang et al, 2021).

### **Studies looking at Altruism/prosocial behaviour**

Studies that used the PEQ to follow up on participants who had taken psychedelics found two results. First, participants self-reported increased levels of prosocial behaviour/altruism. Second, participants either did not report or reported much smaller increases in anti-social/negative social behaviour.

The PEQ looks at self-reported retrospective change. A limitation of this approach is its reliance on participants being able to accurately identify if changes have occurred and to accurately attribute changes to drug experiences.

Many of the studies using the PEQ do not have a parallel long-term control group meaning it is not clear if the subjective changes reported are effects of psychedelics or other non-controlled for factors. Expectations of long-term positive change following psychedelic use could bias participants' responses. Other factors might also influence reports of change. For example, some studies included some element of psychological support such as spiritual guidance (Griffiths et al, 2018), preparatory and post integrative psychotherapy (Ross ,2016) and CBT for smoking cessation (Johnson et al, 2017).

However, studies which did use parallel control groups found the same as studies that did not have control groups. Participants reported increased levels of prosocial behaviour/altruism. They found that these increases were significantly bigger than in the parallel control group, suggesting it was the drug causing the effect. A study (Griffiths et al, 2011) comparing scores on the PEQ after different doses found effects were dose dependent. Participants reported more changes with larger doses of psilocybin. No changes in anti-social/negative social effects were found in either drug or control groups. Using control groups should reduce the impact of reporter bias as participants in both groups should not know whether or not they took the psychedelic. However, because psychedelics have noticeable and well-known effects it is very possible participants would have guessed which group they were in.

Taken together, these results suggest that participants do experience, or think they experience, increases in pro-social behaviour and altruism following psychedelic use.

### **Studies looking at other measures of social functioning**

Two studies (Agin-Liebe et al, 2020 & Griffiths et al, 2018) looked at social functioning by measuring quality of social relationships and interpersonal closeness respectively. Agin-Liebe et al., 2020 found participants reported no significant changes in quality of social relationships when followed up years after psychedelic use despite an upward trend. As is the case with much of the experimental research into psychedelic the sample size used was small meaning it may not be sufficiently powered to pick up changes. Another potential limitation of this study related to the population studied. All participants have life threatening cancer, a diagnosis which may have negative consequences on quality of social relationships. A study with a parallel control group would be able to isolate the drugs effect.

Griffiths et al (2018) found participants who had been given psilocybin reported significantly more interpersonal closeness 7 months after than they did at baseline. However there was no significant difference compared to a control group. However, for a third group of participants (who received psilocybin plus extra support), there was a significant increase in interpersonal closeness reported compared to the placebo group. This poses a question beyond the scope of this review about whether the lasting effects of psychedelics may be mediated by factors such as extra support.

This study also looked at changes in forgiveness, using two different scales to compare baseline measures with 6 months post psilocybin. Only one of these scales (the TRIM-18) showed significant change compared to control group – participants reported increased benevolence motivation (having goodwill for people who transgress) and decreased avoidance motivation (the desire to avoid a transgressor). However on the Trait Forgiveness Scale no changes were found. This could be because the two scales are measuring different things, the TRIM-18 measures state forgiveness, a person's current degree of positive thoughts, feelings and intentions towards an offender (McCullough et al, 1998) whereas the Trait Forgiveness Scale measure conceptualises forgiveness as a stable personality trait and is less sensitive to changes over time (Berry et al, 2005).

## **Summary**

Overall the literature suggests some evidence that classic psychedelics might be associated with lasting improvements in social processing or social functioning. However due to the overall poor quality of the data (with studies being largely uncontrolled, having small sample sizes or relying on retrospective measures) it is impossible to draw any real conclusions or make any clinical recommendations.

Future research should aim to improve the quality of the evidence available and should focus on controlled studies with sample sizes large enough to pick up effects, using both pre and post measures and adequate doses of psychedelic drugs.

The current review suggests psychedelics might have the potential to cause lasting improvements in social processing and functioning and because of the potential positive clinical implications and the personal and social cost of mental health conditions such as depression further research in this area is worth pursuing.

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## **Part 2: Empirical Paper**

Do autistic people attribute perceived change in mental health to a psychedelic experience?

## Abstract

### Background & Aims:

Research suggests that psychedelic drugs may show therapeutic potential in non-autistic populations. The study aims to answer three questions. One, do autistic people attribute any perceived changes in their mental health (depression, anxiety, stress and social anxiety) to their most impactful psychedelic experience. Two, what factors (e.g. quality of psychedelic experience, context they are used in) influence any perceived changes. Three, are any perceived changes in mental health associated with perceived changes in two proposed mechanisms of psychedelic improvement: changes in social connectedness and psychological flexibility.

### Method:

Autistic adult participants who have used a classic psychedelic at least once completed an online survey (N= 233). They were asked about perceived changes in mental health attributed to their most impactful psychedelic experience using adapted versions of the Depression, Anxiety and Stress scale (DASS-21) and the Social Phobia Inventory (SPIN). They were also asked about the quality of their experience using the Mystical Experiences Question (MEQ) and the Challenging Experiences Questionnaire (CEQ) and the safety and supportiveness of the environment and their mindset before taking the drug. Adapted measures looking at two potential mechanisms for change were used to assess reported changes in psychological flexibility (the Acceptance and Action Questionnaire) and social connectedness (Social Connectedness Scale). Regressions were used to determine the association between context and quality of experience and perceived change in mental health. Regression was also used to determine the association between perceived change in sense of connection and psychological flexibility and perceived change in mental health.

### Results:

The majority of participants reported perceived positive changes in depression (n=184/233, 79%), anxiety (144/233, 61.8%), stress (174/233, 74.4%) and social anxiety (178/233, 76.4%) which they attributed to use of a psychedelic drug. Psychedelic-induced mystical experience significantly predicted change in all measures of perceived change in mental health. Both perceived improvements in Psychological flexibility ( $R^2 = 0.52$ ,  $F(1,$

231) = 251.05,  $p < 0.001$ ) and sense of connection ( $R^2 = 0.38$ ,  $F(1,231) = 141.77$ ,  $p < 0.001$ ) were associated with improvements in overall and disorder specific mental health symptoms.

### **Conclusion:**

Evidence supports the observation that psychedelic experiences are associated with perceived improvements in mental health in an autistic population. These improvements appear to be associated with the quality of psychedelic-induced mystical experience and perceived improvements in psychological flexibility and social connectedness. These results suggest there would be rationale for future research into the safety, tolerability, and efficiency of using psychedelics therapeutically for autistic people with mental health conditions.

Include a power calculation in the methods section 1 X

Explain why it was of interest to control for gender and age, and to explore gender incongruence as a factor 4

Clarify the types of drop-out – it appears that many or most of those dropped out did not effectively enrol in the project X

Clarify what BOLD refers to and how it is interpreted. X

In the discussion section briefly expand on the possible mechanisms for mystical experiences impacting on perceived changes in mental health drawing on psychological theories of depression and interventions underpinned by theory X

## **Introduction**

### **Autism and Mental Health**

Autism spectrum disorder (hereafter ‘autism’) is a neurodevelopmental condition characterised by difficulties with social communication and restrictive or repetitive behaviours (American Psychiatric Association, 2013). Although there is no consensus within the autistic community as to which language should be used to describe autism, a UK survey of autistic people and their families found that ‘autistic person’ was often preferred to ‘person with autism’ (Kenny et al, 2015) so this language will be used throughout this study.

Autism and mental health conditions often co-occur. One review by Hollocks et al (2019) found that rates of depression, anxiety disorder and social anxiety in autistic adults are estimated to be 23%, 27% and 29% respectively. Another review found rates of depressive disorders to be 11% and anxiety disorders to be 20% in autistic people (Lai et al, 2019). These rates are higher than in the non-autistic population where estimates are between 1 and 12% (Hollocks et al, 2019).

There are a number of theories that try to explain why mental health conditions and autism commonly co-occur. It could be that the conditions have shared or overlapping symptomology, for example repetitive behaviours are seen in both obsessive compulsive disorder (OCD) and autism (Lai & Baron-Cohen, 2015). It could also be that the two share underlying mechanisms or causes such as genetic predispositions (e.g. Stefanik et al, 2018). Mental health problems could also be understood as consequences of life experiences that go along with autism, for example the experience of living with a stigmatised condition (Fuld, 2018).

Co-occurring mental health problems have been shown to lead to worse outcomes for autistic people. Studies have shown that psychiatric comorbidity is linked to poor global functioning (Gillberg et al, 2016) and that poor mental health mediates the link between autism and poor social adjustment (Chiang et al, 2016). This highlights the importance of good understanding of mental health in autistic populations and the availability of effective treatments or preventative interventions.

## **Psychedelics and Mental Health**

‘Classic’ psychedelics are a class of hallucinogenic drug which act as serotonin 2A receptor (5-HT<sub>2A</sub>R) agonists (Garcia-Romeu et al., 2016). They include drugs such as lysergic acid diethylamide (LSD), psilocybin and N,N-dimethyltryptamine (DMT) and share a capacity to induce changes in consciousness, perceptual processing and affect.

Psychedelic hallucinogens derived from plants have been used for centuries for their psychotropic qualities as part of religious or therapeutic practices (e.g. El-Seedi et al, 2005). In 1938 Albert Hoffman synthesised Lysergic acid diethylamide (LSD) and marketed it for use in adjunction to psychotherapy (Lee and Shlain, 1992). Interest in the potential benefits of hallucinogens for autistic people began in the 1960’s. This initial interest sparked a series of ethically and methodologically problematic studies. For example, autistic children were ‘treated’ using psychedelics (Sigafos et al, 2007) with no mention of parent or child giving consent and no obvious rationale for treatment. Some of these early studies reported improvements in mood, vocabulary and emotional response in autistic children and some reported no changes or negative side effects such as anxiety and depression. It is difficult to draw any clear conclusions from these studies due to methodological problems, for example dependent variables were often not defined and were not objectively measured and outcomes tend to be descriptive accounts of subjective observations. (Sigafos et al, 2007).

Modern research into Psychedelics started in the 1990s. Stassman et al’s (1994) study was the first to administer classic psychedelics after several decades of prohibition in the USA. Modern psychedelic research in non-autistic populations has highlighted the potential of psychedelics to positively impact mental health. A feasibility trial and follow up indicated that psilocybin with psychological support led to a reduction in depressive symptoms for people experiencing treatment resistant depression (Carhart-Harris et al, 2016, 2018). In a randomised control trial, Griffiths et al (2016) found psilocybin produced substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer. A similar randomised control trial found LSD reduced trait anxiety up to 12 months post treatment (Gasser et al, 2014). Additionally, psilocybin has also been shown to have benefits for smoking cessation (Johnson et al, 2014) and OCD (Moreno et al, 2006). However it is important to note the potential limitations of these modern psychedelic studies. Studies tend

to have small sample sizes and be recruited from volunteers who may already have an interest in psychedelics. Research into a much larger sample people self-medicating with psychedelics shows people report benefits to their mental health. A questionnaire looking at a people self-medicating by using psychedelics found that they reported self-administered psychedelic treatment was more efficacious and had higher symptom reduction and more quality of life improvement when compared to other treatments offered by a medical professional (Mason & Kuypers, 2018).

To date, no experimental studies have investigated the impact of psychedelics on mental health in an autistic sample. However, several studies have looked at the use of 3,4-Methylenedioxymethamphetamine (MDMA), a type of hallucinogen called an empathogen which shares the capacity to induce changes in consciousness, perceptual processing and affect (Garcia-Romeu et al, 2016). In a randomised controlled trial comparing MDMA with a placebo, autistic people saw their social anxiety decrease more after receiving two eight hour sessions of psychotherapy plus MDMA than when receiving the psychotherapy sessions plus placebo (Danforth et al, 2018).

### **How might psychedelics effect mental health in autistic people?**

One way psychedelics may improve mental health is by increasing feelings of social connection. Social connectedness, a psychological sense of belonging, has been linked to psychological wellbeing. For example it has been shown to be related to reduced trait anxiety and increased state self-esteem (Lee & Robbins, 2008). A study looking at associations between social predictors of depression in college students found that social connectedness mediated the link between other social predictors of such as social support and competence and reduced symptoms of depression (Williams & Galliher, 2006). A systematic review found that improved connectedness played a key part of recovery for mental illness (Leamy et al, 2011).

A link between psychedelics-related connectedness and positive mental health outcomes has been substantiated by Carhart-Harris 2016's trial of psilocybin as an intervention in treatment resistant depression. The researchers proposed that a sense of "connection" was key to the treatment's success (Carhart-Harris et al, 2018) and a qualitative follow up study to the trial by Watts et al (2017) identified 'a change from feeling socially disconnected to connected', as one of two potential processes of change following

psychedelic use. Many of the participants reported that a sense of connectedness featured acutely (whilst experiencing the immediate and noticeable effects of the drugs) and lasted for the weeks and months after the treatment (Watts et al, 2017). Researchers also found connectedness was important in a study amongst an autistic population using MDMA. 91% of respondents to a survey reported an increase in empathy and sense of social connection and a smaller number (12%) found this effect lasted more than two years (Danforth, 2013). These studies suggest that psychedelics have the potential to increase a sense of connection and that this may have positive effects on mental health.

These positive effects of psychedelics may be especially important for people who lack a sense of connection. Difficulty in connecting with others is one of the key disabling aspects of autism. A review found that amongst 19 studies, all but one found a significant reduction in social connectedness in autistic compared to non-autistic children (Diendorfer et al, 2021). Furthermore, there is evidence that a lack of social connectedness may increase risk for autistic people of developing mental health problems. Schiltz et al (2020) found loneliness and social isolation mediated the link between autism and mental health. Stice & Lavner (2019) also found that the connection between autism and anxious and depressive symptoms were mediated by social connection with lower social connection predicting negative mental health outcomes. This suggests that improving connection for autistic people could have a positive impact on mental health and psychedelics, therefore, may be an efficacious intervention.

In the current clinical literature, another commonly proposed potential mechanism for post-psychedelic change is through an increase in psychological flexibility. Being psychologically flexible can be defined as a person being connected with both their current internal psychological state and with the present environment which allows the flexibility to be able to both change or persist with behaviours which bring about valued ends and to not be overcome or accept interferences (Hayes et al, 2011). The opposite of flexibility is experiential avoidance where behaviour is guided by psychological reactions/feelings (Bond et al, 2011). This describes a pattern when behaviour is controlled by internal experiences such as feelings and thoughts or the desire to avoid these experiences. In qualitative research non-autistic participants describe improved psychological flexibility being associated with an improvement in mental health. Participants who took part in a psilocybin trial described experiencing a change from a desire to avoid difficult emotions to a willingness to accept them (Watts et al. 2017).

A meta-analysis of 27 studies using a measure of psychological flexibility, the Acceptance and Action questionnaire (AAQ-2) (which asks about emotional avoidance and the impact of emotional avoidance) on a non-autistic sample found it predicted mental health outcomes such as improvement in depression, anxiety as well as general mental health (Hayes et al, 2006). In a study using a cross-sectional survey to retrospectively assess the association between improvements in psychological flexibility and improvements in mental health, psychological flexibility has been shown to mediate the positive impact of psychedelics on depression and anxiety in a non-autistic population (Davis et al, 2020).

Autistic people may be more likely to struggle with psychological flexibility. There has been shown to be a link between intolerance of uncertainty and mental health problems in autistic children (Boulter et al, 2014). Intolerance of uncertainty can be defined similarly to psychological flexibility as the belief that unexpected events are negative and to be avoided and finding it different to function when faced with unexpected events (Buhr & Dugas, 2002). One of the key dimensions that underlies intolerance of uncertainty is the idea of being cognitively or behaviourally ‘stuck’ (Birrell et al, 2011). A pilot study using Acceptance and Commitment Therapy (ACT), a therapy designed to target psychological flexibility in an autistic population found that participants’ psychological flexibility improved. As consequence of this improvement in psychological flexibility, quality of life also improved (Pahnke et al, 2019). Therefore, psychological flexibility could be a potential mechanism to improve mental health in autistic people. As psychedelics may increase psychological flexibility, they may also have the potential to improve mental health.

### **What might predict outcomes from psychedelics?**

In order to improve outcomes for psychedelic-assisted mental health treatments, researchers have investigated what factors might predict responses to psychedelics (e.g. Haijen et al, 2018). For example, the Mystical Experience Questionnaire was developed to assess the quality of the psychedelic experience in terms of its ‘mysticalness’. In non-autistic samples, a higher degree of mystical experience has been shown to be associated with positive therapeutic outcomes (e.g. Griffiths et al, 2006 & Griffiths et al, 2016) however there is no research on autistic people.

Other factors may predict responses to psychedelic drug use, such as how ‘challenging’ the experience was. How ‘challenging’ the experience was did not predict change in wellbeing but was shown to be related to the mindset prior to taking the drug, the intentions of the person taking it and the setting where it took place (Haijen et al, 2018). Studerus et al (2012) pooled data from 23 controlled studies to identify non-pharmacological factors which predict how people experience the immediate effects of psilocybin and found that non-pharmacological factors, such as having experienced few psychological problems in the previous few weeks and being in an emotionally excitable and active state, impacted on the degree of mystical experience.

Therefore, the context (e.g. where, when and in what circumstance) psychedelics are used in is an important factor in determining responses. Carhart-Harris et al (2018) argue that context is of critical importance due to its influence on the quality of the acute experience (for example mystical experience) which has been shown to predict therapeutic outcome. There is no research on the importance of contextual factors for predicting responses to psychedelics in an autistic population.

## **Research Questions**

The evidence summarised above suggests a lack of research on the effects of psychedelics for autistic people and the potential lasting effects on mental health. As psychedelics have shown clinical potential for non-autistic people it would be useful to know whether the same is true for autistic people. If so this could support a rationale for a program of work investigating the potential for these drugs to be used clinically.

This study aims to understand self-reported effects of psychedelics on mental health experienced by autistic people. It seeks to answer the following questions:

1. Do autistic people attribute any perceived changes in their mental health (depression, anxiety, stress and social anxiety) to their most impactful psychedelic experience?
2. Are any perceived changes in mental health attributed their most impactful psychedelic experience associated with the reported quality and context of the psychedelic experience? Specifically I ask:

- a. Is the reported degree of psychedelic-induced mystical experience associated with perceived changes in mental health?
  - b. Is the reported challengingness of the experience associated with changes in mental health.
  - c. Do contextual variations such as the supportiveness of the context and a person's mindset before taking psychedelics impact on perceived changes in mental health?
3. For autistic people, does their most impactful psychedelic experience result in perceived changes in sense of connection and psychological flexibility, and do these improvements have a perceived impact on change in mental health.

## **Method**

### **Study design**

To answer the stated research questions, this study adopts a cross-sectional within-subjects design. It uses an internet-based survey to retrospectively assess perceived change in mental health attributed to a selected experience where a classic psychedelic drug was used in an autistic population. Similar methodology has been used in previous studies to explore lasting effects of psychedelic use (e.g., Carbonaro et al, 2016) and to assess retrospective change (Davis et al, 2020). Descriptive statistics were used report participants perceived change and multiple regression analysis was used to explore the relationships between predictor and outcome variables whilst controlling for potential co-varying or confounding variables. This study was part of a joint project conducted with Jack Stroud (Stroud, 2022) see appendix 2 for further details on how the project was split.

### **Participants**

#### ***Recruitment***

Participants were a self-selecting sample recruited online who learnt of the study through adverts on social media (e.g., Facebook, Twitter, Instagram), relevant online forums (e.g., reddit), shares through friends and family and word of mouth. Participants were also recruited through E-mails sent to members of the ‘Autistic Psychedelic Community’ via their mailing list and adverts on their website. Interested participants followed a link to the survey and were directed to the participant information sheet. After reading the information sheet they were asked if they consented to taking part in the study. Once consented participants were asked a series of questions to make sure they met the below inclusion criteria (See appendix 3 for exact wording).

#### ***Inclusion/Exclusion Criteria***

To take part in the study participants had to be over 18, have a diagnosis of or self-identify as autistic, be proficient in the English language and have taken a ‘classic psychedelic’ (here defined as hallucinogenic drug which acts as a serotonin 2A receptor (5-HT<sub>2A</sub>R) agonist (Garcia-Romeu et al., 2016. )). Drugs that were included were psilocybin, lysergic acid diethylamide (LSD), Ayhuasca, Peyote, N, N-dimethyltryptamine (DMT), 5-MeO-DMT and D-lysergic acid amide (LSA) (see appendix 4 for full drug list). Participants

had to complete all questions and then submit to confirm they consent to taking part in the study. If questions were not completed or submitted they were deleted without being analysed.

## **Measures**

### ***Demographics***

To understand the characteristics of the sample demographic information on age (in years), gender identity, ethnicity, education level and country of residence was collected. Gender identity was used rather than binary gender to reflect the large amount of autistic people who identify outside of the binary of man or women (Warrier et al., 2020).

### ***Autism***

Current features of autism were assessed using a 10-item version of the Autism Spectrum Quotient (AQ-10, Hoekstra et al., 2011). This is a shortened version of the original 50 item Autism Spectrum Quotient (AQ, Baron-Cohen et al., 2001) which has been shown to be significantly elevated in people with a diagnosis of an autism spectrum condition (ASC) (Baron-Cohen et al., 2001). The shortened version has been shown to have an acceptable to good internal consistency ( $\alpha$  between .77 and .86) and correlates very highly ( $r$  between .93 and .95) with the validated full-scale AQ (Baron-Cohen et al., 2001). It is used as a brief tool to screen for autism.

We also asked participants if they had been diagnosed as autistic by a health professional and if so what kind of professional made the diagnosis. Participants were asked the wording of their diagnosis (e.g. Asperger Syndrome or autism spectrum disorder) and how old they were when they received the diagnosis. Participants who were not diagnosed by a health professional were asked if they self-diagnose or self-identify as autistic. People who self-diagnosed as autistic were included in the sample as due to barriers in accessing diagnosis this may represent a truer sample of autistic adults. T-tests were used to compare participants who were diagnosed by a professional and participants who self-identify as autistic on the AQ-10 and all predictor and outcome variables.

### ***Current Mental health***

Participants were asked about their current and mental health. They were asked to select current conditions from a list including depression, psychosis, social anxiety disorder

(SAD), post-traumatic stress disorder (PTSD), obsessive compulsive disorder (OCD), panic disorder, generalised anxiety disorder (GAD), bipolar disorder, eating disorder, sleep disorder, substance abuse disorder, ADHD and a free text option to write in any other relevant disorders (See appendix for full list).

### ***Drug use and experience***

Participants were asked to recall the psychedelic experience which they felt had the most impact on their lives. If they had multiple experiences, they were asked to select and rate for the more impactful experience only and all questions should be answered in relation to that experience only. They were asked what drug/drugs they took along with when the experience happened (how many years ago).

### ***Set***

Questions adapted from Haijen et al (2018) were used to be used to retrospectively assess the participants mindset ‘set’ before taking the drug. Participants were asked to respond to each of the items with how much they agree with statements such as “I was in a good mood” and “I felt comfortable about the upcoming experience” using a 5-point scale ranging from “1 – strongly agree” to “5 – strongly disagree”. Answers to nine questions were combined to give a total score indicating how ‘good’ a mindset participants had before their most impactful psychedelic experience was with lower total scores representing a better mindset.

### ***Setting***

Questions adapted from Haijen et al (2018) were used to retrospectively assess the quality of the setting the drug was taken in such as the perceived safety and supportiveness of the setting. Participants were asked to respond to each of the items with how much they agree with statements such as “The setting in which the experience took place was physically safe” and “The setting in which the experience took place was supportive” using a 5-point scale ranging from “1 – strongly agree” to “5 – strongly disagree”. Answers were combined giving a total score indicating how ‘good’ (how supportive and safe) the setting was. Lower numbers suggest a ‘better’ setting.

### ***Mystical Experience Questionnaire (MEQ)***

In reference to their most impactful experience participants then completed the 30-item Mystical Experience Questionnaire (MEQ, Barrett et al, 2015). The MEQ is self-report measure designed to assess the extent and nature of mystical experiences that occur after psychedelic use (Maclean et al, 2012). Participants were asked to respond to each of the MEQ30's items which ask if they experience phenomena such as "a sense of reverence" and an "experience of amazement" using a 6-point scale ranging from "0 -None; not at all" to "5 - Extreme (more than any other time in my life and stronger than 4)". A higher score on the MEQ suggests a higher degree of mystical experience.

The total score is indicative of the overall intensity of mystical experience and was used in the analysis to represent the variable 'degree of mystical experience' as related to a participants chosen psychedelic experience. A 'complete' mystical experience was implicated if a score of at least 60% of the maximum total scale was obtained (Barrett et al, 2015) The measure shows good reliability and validity when used with psychedelic drug users (Maclean et al, 2012).

### ***Challenging Experience Questionnaire (CEQ)***

The 26-item Challenging Experience Questionnaire (CEQ, Barrett et al, 2016) was used in reference to participants most impactful experience. The CEQ is a self-report measure designed to measure the level of immediate adverse psychological reactions to psychedelics (what might be colloquially know as 'bad trips'). Participants were asked to respond to each of the CEQ's items which ask if they experience phenomena such as an "experience of fear" and "isolation and loneliness" using a five point scale ranging from "0, none, not at all" to "4, extreme, more than ever before in my life". The total score is indicative of the amount of adverse psychological reactions participants report with higher scores representing a more challenging experience (Barrett et al, 2016). The measure shows good reliability and validity when used with psychedelic drug users (Barrett et al, 2016).

### ***Perceived changes in mental health***

Perceived changes in mental health symptoms were measured using versions of validated measures assessing current symptoms of mental health problems that have been adapted to measure retrospective change. Participants were asked to recall their most impactful psychedelic experience and rate change in symptoms they perceived to be to be linked to that experience. Answers were scored on an 11-point scale from -5 to 5 with negative numbers representing a reduction in symptoms (with smaller numbers representing a

greater reduction in symptoms), positive numbers representing an increase in symptoms (with larger numbers representing a greater increase in symptoms) and zero representing no change.

Wordings of questions were kept as close as possible to the original but were changed to reflect retrospective change. Adapted measures can be seen in appendix 4.

### ***Depression, anxiety and stress***

Perceived changes in symptoms of depression, anxiety and stress were assessed by a version of the Depression, Anxiety & Stress Scale (DASS-21, Ng et al, 2007) adapted to measure retrospective change. The scale was changed from asking about current symptoms of depression, anxiety and stress to asking about perceived change in symptoms attributed to their selected psychedelic experience. The DASS-21 consists of 21 questions with three subscales; depression, anxiety and stress.. The DASS has been shown to demonstrate good construct validity and internal consistency as is seen as a reliable tool to use in research (Henry & Crawford, 2005) however it is not known how the adaptations may impact reliability and validity.

### ***Social Anxiety***

An adapted version of the 17 item Social Phobia Index (SPIN, Connor et al, 2000) was used to measure retrospective changes in social anxiety. The Social Phobia Inventory (SPIN) was found to have good convergent validity and has been shown to be a valid and reliable tool (Mahdi, 2006). It is however unclear whether the validity and reliability changes when adapted for retrospective use.

### ***Social Connection***

Perceived changes in social connection were assessed by an adapted version of the Social Connectedness Scale (SCS, Lee and Robbins, 1995). In its original form, the SCS has good validity and reliability (Lee and Robbins, 1995). This scale was scored in the same way as the DASS-21 and SPIN, on a 11-point scale measuring with positive and negative changes.

### ***Psychological Flexibility***

Perceived changes in cognitive flexibility were measured using an adapted version of the Acceptance and Action Questionnaire II (AAQ-II; Bond et al, 2011). In its original form, the AAQ-II has good validity and reliability (Bond et al, 2011).

## **Ethics**

Ethical approval for the study was obtained through the University College London (UCL) Research Ethics Committee (Project ID: 20251/001 - see appendix 1). A risk assessment was completed prior to data collection.

Data was collected from participants was pseudonymised. Because the full dataset contains demographic details such as age in years, gender identity, ethnicity, education level, country of residence, autism and mental health diagnosis, there may be a small risk of indirect identification through a combination of chance and the use of multiple demographic characteristics. However, because we did not collect data such as date of birth or IP addresses any identification would always be probabilistic rather than definitive.

To keep data as secure as possible it was stored on UCL drives and was password protected. Access to data was only available to those working directly on the project. A UCL Data Protection Impact Assessment (DPIA) was completed before starting data collection. All researchers working on the project completed UCL General Data Protection Regulation (GDPR) training prior to accessing the data.

Because the survey does ask questions about mental health along with potentially distressing Psychedelic experiences the survey included a link to an information seek with advice on how to seek support (see appendix 6).

## **Missing data**

All participants completed all key predictor and outcome variables measures. Due to the design of the survey participants had to complete all of these measures in order to complete the survey and submit their responses. Not all participants provided demographic data and three participants did not complete demographic data. For other descriptive data (for example information about autism diagnosis) information about missing data is included in tables in the results section.

## **Data analysis**

To describe the sample, descriptive statistics (means, standard deviations, frequencies, and percentages) were used, using participants answers to demographic questions.

To answer research question 1, descriptive statistics (means, confidence intervals, frequencies, percentages and distribution graphs) were calculated to show participants' perceived change in mental health using the adapted DASS total, DASS depression subscale, DASS anxiety subscale, DASS stress subscale and SPIN. Answers to questions about retrospective change were scored on an 11-point scale from -5 to 5 with negative numbers representing a reduction in symptoms (with smaller numbers representing a greater reduction in symptoms), positive numbers representing an increase in symptoms (with larger numbers representing a greater increase in symptoms) and zero representing no change. To calculate percentage of participants who reported improvements, deterioration, or no change an average answer was calculated and those who scored on average above zero were deemed to have deteriorated, those who on average scored zero were deemed to have not changed and those who scored below zero to have improved.

To answer research question 2, descriptive statistics and multiple regression analyses were used. Firstly, descriptive statistics (means, confidence intervals and distribution graphs) were calculated to show reported levels of predictor variables (psychedelic-induced mystical experiences, challengingness of experience and set and setting). Secondly univariate linear regressions were performed to assess the relationship between predictor variables (psychedelic-induced mystical experiences, challengingness of experience and set and setting) and outcome variable (perceived change in depression, stress and anxiety and social anxiety). A multivariate model was also used to control for baseline covariates (age and gender) and all hypothesis led predictors (psychedelic-induced mystical experiences, challengingness of experience and set and setting). Baseline covariates were controlled for to help rule them out as potential confounding variables. Previous research has shown that age (Prior et al, 2020) and gender (Astbury, 2001) can predict mental health outcomes

To answer research question 3, descriptive statistics and multiple regression analyses were used. Firstly, descriptive statistics (means, confidence intervals and distribution graphs) were calculated to show reported levels of predictor variables (psychological flexibility and social connectedness). Secondly univariate linear regressions were performed to assess the

relationship between predictor variables (psychological flexibility and social connectedness) and outcome variables (perceived change in depression, stress and anxiety and social anxiety). A multivariate model was also used to control for baseline covariates (age and gender).

All analysis were conducted using JASP version 0.16.2 (JASP Team (2022)).

### **Power Calculation**

Alpha (probability of a false positive) set to 0.05

Power = (1-beta), beta is set to .80 (probability of a false negative)

Expected effect size = since there are no directly relevant published studies in this area, we have decided that we will estimate a Cohen's  $d = 0.4$  as this is considered a reasonable estimate for the smallest effect size of interest in psychological research. We transformed Cohen's  $d$  into  $f$  in accordance with Cohen (1988), Rosenthal (1994, S. 239), using this website: [https://www.psychometrica.de/effect\\_size.html](https://www.psychometrica.de/effect_size.html).

The calculated effect size was  $f = 0.2$   $f^2 = 0.04$  Solved for  $n$  using G\*Power a priori power analysis: Statistical test = Linear multiple regression: fixed model, R<sup>2</sup> deviation from zero Effect Size  $f = 0.02$  Alpha = 0.05 Power (1-Beta) = 0.80 Number of predictors = 1 (mystical experience or psychological flexibility or connection).

$N =$  minimum 199.

## Results

### Sample characteristics

#### *Demographics*

Out of the 960 people who clicked on the survey 284 participants completed the survey and submitted their responses. Data was collected from a total of N = 233 participants who met inclusion criteria (51 participants were excluded due to not having taken a classic psychedelic). Demographic information for participants is presented in table 2.1.

**Table 2.1**

#### *Demographic information*

<b>N = 233</b>	<b>Mean, (SD), Range</b>
<b>Age</b>	29.8 (9.25) 18-67
<hr/>	
<b>Frequency (Percentage%)</b>	
<hr/>	
<b>Gender</b>	
Woman	55 (23.61)
Man	113 (48.50%)
Trans Woman	3 (1.23%)
Trans Man	3 (1.23%)
Non-binary	49 (21.03%)
Other	9 (3.86%)
No data	1 (0.43%)
<b>Nationality</b>	
United States	111 (47.64%)
United Kingdom	46 (19.74%)
Other European	35 (15.02%)
Canada	23 (9.87%)
Australia	12 (5.15%)
Other	3 (1.29%)
No data	3 (1.29%)
<b>Education</b>	
Until Age 16	14 (6.01%)
Until Age 18	74 (31.76%)

Bachelors degree (or equivalent)	90 (38.63%)
Masters degree (or equivalent)	38 (16.31%)
Doctoral degree (or equivalent)	8 (3.43%)
None of the above	8 (3.43%)
No data	1 (0.429%)

**Ethnicity**

White	194 (83.26%)
Mixed	23 (9.87%)
Asian	5 (2.15%)
Black	1 (0.43%)
Other	8 (3.43%)
No data	2 (0.86%)

**Drugs used during most impactful psychedelic experience**

All participants used at least one classic psychedelic as part of their most impactful psychedelic experience. Information about the classic psychedelic used, drugs used in combination and when the most impactful experience happened used are presented in table 2.2.

**Table 2.2**

*Information about drug used in the most impactful psychedelic experience*

N = 233	Frequency (Percentage %)
<b>Classic Psychedelic Drug Used</b>	
LSD	102 (43.78%)
Psilocybin	85 (36.48%)
Ayahuasca	9 (3.86%)
DMT	11 (4.72%)
Peyote	1 (0.43%)
5-Me0-DMT	2 (0.86%)
Morning Glory	3 (1.29%)
More than one Classic Psychedelic	20 (8.58%)
<b>Drug Combination</b>	
Classic Psychedelic Drug Only	113 (48.50%)
Classic Psychedelic + MDMA	7 (3.01%)

Classic Psychedelic + Ketamine	4 (1.72%)
Classic Psychedelic + Non Classic Psychedelic	2 (0.86%)
Classic Psychedelic Drug + Cannabis	61 (26.18%)
Classic Psychedelic + MDMA + Cannabis	10 (4.29%)
Classic Psychedelic + Ketamine + Cannabis	3 (1.29%)
Classic Psychedelic + Ketamine + MDMA + Cannabis	4 (1.72%)
Multiple Classic Psychedelics only	5 (2.15%)
Other combinations	24 (10.30%)
	<b>Mean (SD)</b>
<b>How long ago was the most impactful experience? (in years ago)</b>	3.99 (6.39)

## Autism

All participants reported to have either been diagnosed with autism or to self-identify as autistic. The Autism Spectrum Quotient (AQ10) was used to assess current autism with scores of 6 or above suggesting potential autism. Information about participants autism diagnoses are presented in table 2.3. In this sample Men and Women were both had similarly likely to have a professional diagnosis of autism (65.6% and 60% respectively) compared to non-binary and trans participants who were less likely to have a professional diagnosis of autism (with rates of 44.9% and 33.3% respectively). T-tests showed no significant difference ( $t(231) = 0.07, p = 0.94$  between the 136 participants who were professionally diagnosed as autistic ( $M = 7.31$   $SD = 2.10$ ) compared to the 97 participants who self-identify as autistic ( $M = 7.29$   $SD = 1.95$ ) on the AQ-10. T-tests comparing the participants who were diagnosed and who self-diagnosed found no differences on any of the outcome measures or main predictors (see appendix 5 for t-test results).

**Table 2.3**

*Autism Information*

	<b>Frequency (Percentage%)</b>
<b>Diagnosed or self-identify? N = 233</b>	
Professional diagnosis	136 (58.37%)
Self Identify	97 (41.63%)

**Who diagnosed? N = 136**

Psychiatrist	43 (31.62%)
Paediatrician	4 (2.94%)
Clinical Psychologist	46 (33.82%)
Team	17 (12.50%)
Other	8 (5.88%)
Not Sure	14 (10.29%)
No data	4 (2.94%)

**Diagnosis Wording N = 136**

Autism	7 (5.15%)
Autism Spectrum Disorder	48 (35.29%)
Autism Spectrum Condition	5 (3.68%)
Asperger's Syndrome	53 (38.97%)
Pervasive Developmental Disorder	5 (3.68%)
Other	7 (5.15%)
Not Sure	10 (7.35%)
No data	1 (0.74%)

**AQ10 N = 233**

Scores ≥ 6	185 (79.40%)
Scores <6	48 (20.60%)
	<b>Mean (SD)</b>
Total score	7.3 (2.03)

---

**Notes:** Autism Spectrum Quotient - AQ10

**Current Mental Health.**

The majority of participants reported at least one current mental health problem (N = 206, 89.70%). Information about mental health was completed by 230 participants with missing data for 3 (1.29%). Information about current mental health is presented in table 2.4.

**Table 2.4***Current Mental Health*

<b>N = 230</b>	<b>Frequency (Percentage %)</b>
<b>Current Mental Health diagnosis</b>	
Yes	206 (89.70%)
No	24 (10.30%)

**Mental Health diagnosis**

Depression	81 (34.76 %)
Psychosis	4 (1.72%)
Social Anxiety Disorder (SAD)	72 (30.90%)
Post Traumatic Stress Disorder (PTSD)	71 (30.47%)
Obsessive Compulsive Disorder (OCD)	32 (13.73%)
Panic Disorder	8 (3.43%)
Generalised Anxiety Disorder (GAD)	80 (34.34%)
Bipolar Disorder	16 (6.87%)
Eating Disorder	18 (7.73%)
Sleep Disorder	46 (19.74%)
Substance Use Disorder	28 (12.02%)
Attention-deficit/hyperactivity disorder (ADHD)	129 (55.37%)
Not Sure	20 (8.58%)
Other	45 (19.31%)
None of the Above	24 (10.30%)

**Research question one: Do autistic people attribute any perceived changes to their mental health to their most impactful psychedelic experience?**

On average participants reported a perceived reduction in symptoms of depression, anxiety and stress (as measured by the adapted DASS total, DASS depression, DASS anxiety, DASS stress) and social anxiety (as measured by the adapted SPIN). Information about perceived change in mental health attributed to most impactful psychedelic experience is presented in table 2.5 and figure 2.1.

**Table 2.5**

*Perceived change in Mental Health – Descriptive Data*

<b>N = 233</b>	<b>Mean</b>	<b>95% Confidence Interval</b>	<b>Frequency (Percentage) of participants reporting perceived improvement</b>	<b>Frequency (percentage) of participants reporting no perceived change</b>	<b>Frequency (Percentage) of participants reporting perceived deterioration</b>
<b>DASS Depression</b>	-1.71	[-1.95, -1.48]	184 (78.97%)	23 (9.87%)	26 (11.16%)

<b>DASS Anxiety</b>	-0.53	[-0.65, -0.41]	144 (61.80%)	42 (18.03%)	47 (20.17%)
<b>DASS Stress</b>	-1.10	[-1.29, -0.98]	174 (74.68%)	27 (11.59%)	32 (13.73%)
<b>DASS Total</b>	-1.11	[-1.27, -0.95]	191 (81.97%)	16 (6.87%)	26 (11.16%)
<b>SPIN Total</b>	-0.98	[-1.16, -0.8]	178 (76.39%)	30 (12.88%)	25 (10.73%)

Mean scores range from -5 to 5 with 95% confidence intervals that are below (and do not cross) zero suggesting a perceived reduction in symptoms, confidence intervals that are above (and do not cross) zero suggesting an increase in symptoms and zero suggesting no change. Lower numbers suggest bigger reductions in symptoms.

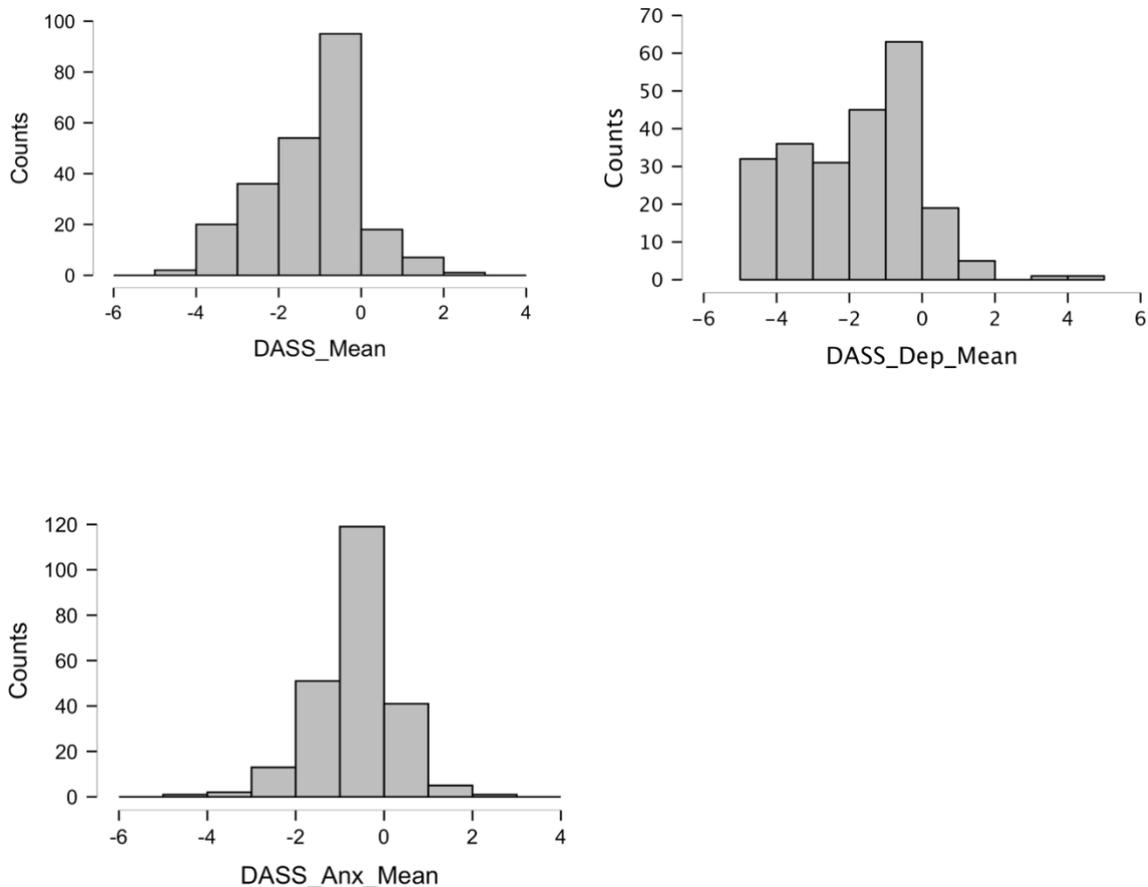
Frequency of participants reporting perceived improvement shows the frequency and percentage of participants reporting improvement rather than no change or worsening of symptoms. Frequency of participants reporting perceived deterioration shows the frequency and percentage of participants reporting deterioration rather than no change or improvement in symptoms. Frequency of participants reporting perceived no change shows the frequency and percentage of participants reporting no change rather than improvement or worsening of symptoms.

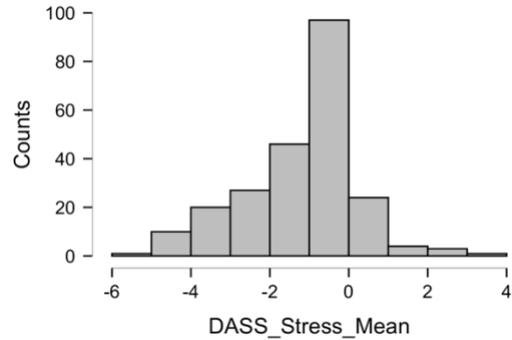
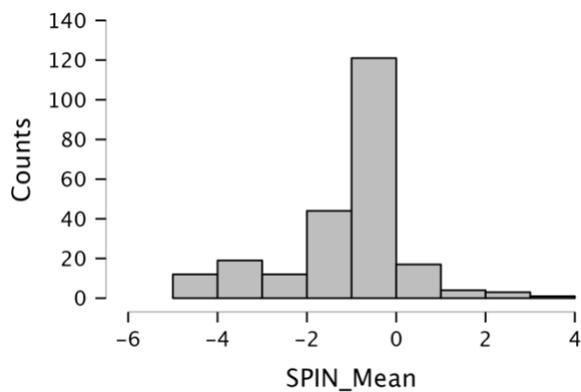
DASS = Depression, Anxiety and Stress Scale

SPIN = Social Anxiety Inventory

**Figure 2.1**

*Histograms showing distribution density for perceived change in mental health*





**Research Question 2: Are any perceived changes in mental health attributed to participants most impactful psychedelic experience associated with the reported quality and context of the psychedelic experience?**

Participants completed four measures assessing the quality of their most impactful experience (how mystical and challenging it was) and the context (the mindset ‘set’ and the setting). 60.52% of participants reported a ‘complete’ mystical experience. On the CEQ participants scored on average a mean of 28.79, a similar level reported in other studies survey in a German population (where the mean was 27.60) (Dworatzky et al, 2022).

Table 2.6 presents descriptive statistics from the MEQ, CEQ and set and setting scales and figure 2.2 one shows distributions.

**Table 2.6**

*Context and Experience – Descriptive Data*

N = 233	Mean	95% Confidence Interval
Mystical Experience Questionnaire (MEQ)	95.25	[90.88, 99.62]
Challenging Experiences Questionnaire (CEQ)	28.79	[25.42, 32.16]

Setting	7.74	[7.31, 8.17]
Set	21.06	[20.43, 21.69]

	Frequency	Percentage
Participants reported a ‘complete’ mystical experience	141	60.52%

MEQ is scored out of 150. Higher numbers suggest a more ‘mystical experience’. A score of over 90 constitutes a ‘complete’ mystical experience.

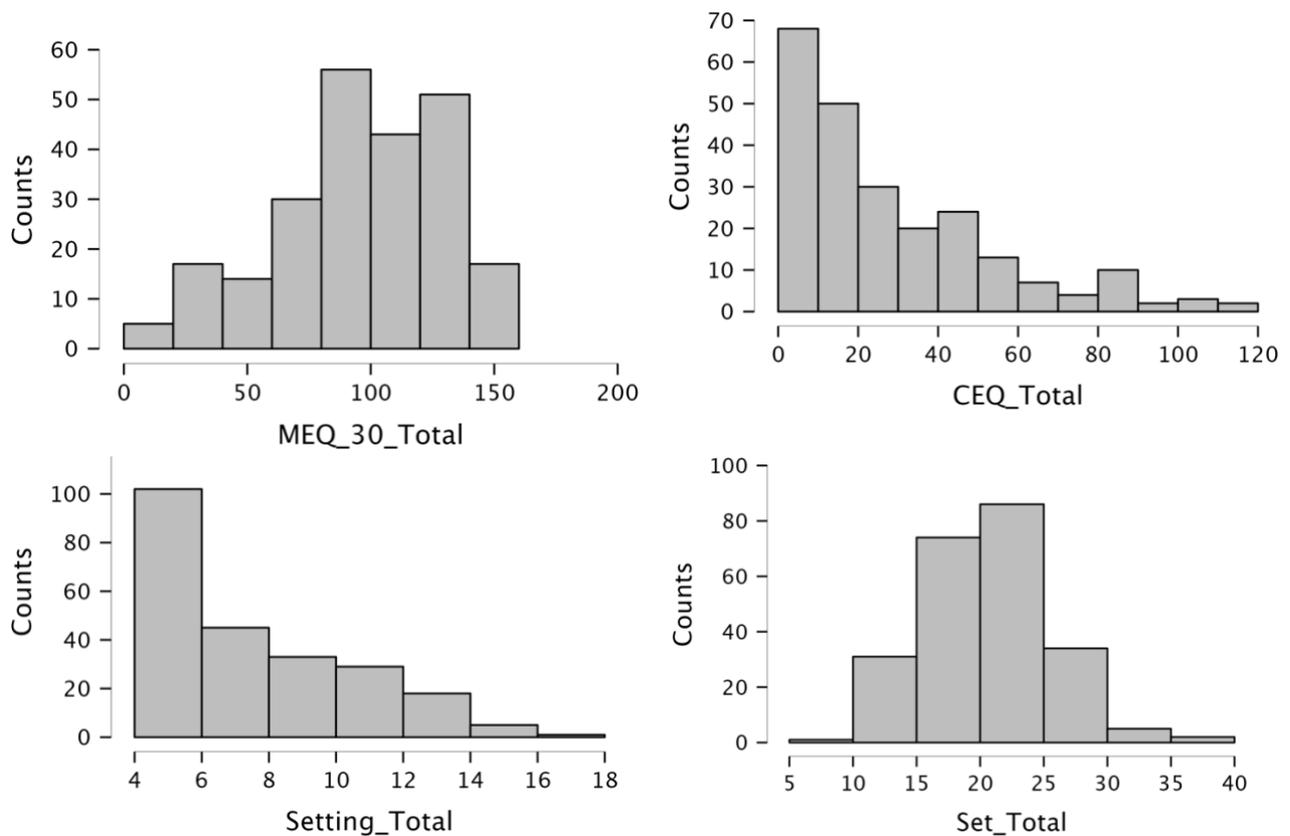
CEQ is scored out of 130. High numbers suggest a more ‘challenging experience’.

Setting is scored out of 20. High numbers suggest a less supportive setting.

Set is scored out of 45. High numbers suggest a worse mindset. Scores of over

**Figure 2.2**

*Histograms showing distribution densities for measures of context and quality of experience*



Unadjusted linear regressions show that the degree of mystical experience (MEQ), the challengingness of the experience (the CEQ), the person’s mindset before taking the psychedelic (set) and identifying as a gender other than male or female significantly predict perceived change in change in depression, anxiety and stress (DASS total).

Unadjusted linear regression of mystical experience (MEQ) scores on the perceived change in in depression, anxiety and stress (DASS total) indicated a significant positive association  $F(1,231) = 32.70$ ,  $p < 0.001$ , with MEQ explaining 12.4% of the variance. A more ‘mystical’ experience was associated with a bigger reduction in perceived symptoms of depression, anxiety and stress. Unadjusted linear regression of challenging experience (CEQ) scores on perceived change in in depression, anxiety and stress (DASS total) indicated a significant positive association  $F(1,231) = 4.153$ ,  $p < 0.05$ , with CEQ explaining 1.8% of the variance in change in mental health scores. A less ‘challenging’ experience was associated with a bigger reduction in perceived symptoms of depression, anxiety and stress. Unadjusted linear regression of mindset prior to drug use (set) scores perceived change in in depression, anxiety and stress (DASS total) indicated a significant positive association  $F(1,231) = 9.04$ ,  $p < 0.01$ , with Mindset explaining 3.8% of the variance in change in mental health scores. A better ‘mindset’ before taking psychedelics was associated with a bigger reduction in perceived symptoms of depression, anxiety and stress.

However once the model was adjusted to control for demographic factors (age and gender) and other potentially covarying predictors (MEQ, CEQ, setting and set) only the degree of mystical experience (MEQ) is significantly associated with change in perceived symptoms of depression, anxiety and stress (DASS total) ( $p < .001$ ).

Table 2.7 presents both unadjusted and adjusted regression coefficients. Regressions for other outcome measure (DASS depression, DASS anxiety, DASS stress, SPIN) can be found in the appendix.

**Table 2.7**

*Unadjusted and Adjusted Regressions for Predicting Perceived Change on DASS (total)*

Variable	Unadjusted		Adjusted					
	B	95% CI	$\beta$	p	B	95% CI	$\beta$	p
<b>Predictors</b>								
MEQ	-0.28	[-0.37, -0.18]	-0.35	< .001	-0.27	[-0.37, -0.17]	-0.35	<0.001
CEQ	0.14	[0.01, 0.27]	0.13	< 0.05	0.13	[-0.02, 0.27]	0.12	0.08
Setting	0.75	[-0.29, 1.79]	0.09	0.16	0.22	[0.80, 1.25]	0.03	0.67
Set	1.05	[0.36, 1.74]	0.19	<0.01	0.09	[-0.73, 0.90]	0.02	0.83
<b>Demographics</b>								
Age	0.26	[-0.12, 0.63]	0.09	0.18	0.26	[-0.09, 0.61]	0.09	0.14

Female (vs Male)	-2.09	[-10.67, 6.47]	-	0.63	-1.66	[-9.94, 6.61]	-	0.69
Other (vs Male)	-8.70	[-16.86, -0.54]	-	< 0.05	-6.92	[-14.72, 0.87]	-	0.08

Note:

MEQ = Mystical experiences questionnaire

CEQ = Challenging experiences questionnaire

Adjusted model includes MEQ, CEQ, Setting, Set, age and gender. R2 = 0.16 N = 232

**Research Question 3: For autistic people, does their most impactful psychedelic experience result in perceived changes in sense of connection and psychological flexibility, and do these have a perceived impact on change in mental health.**

Participants reported perceived increases in both Psychological Flexibility and Connection. Table 2.8 presents descriptive statistics from these measures and figure 2.3 shows distributions.

**Table 2.8**

*Perceived change in Psychological Flexibility and Connection – Descriptive data*

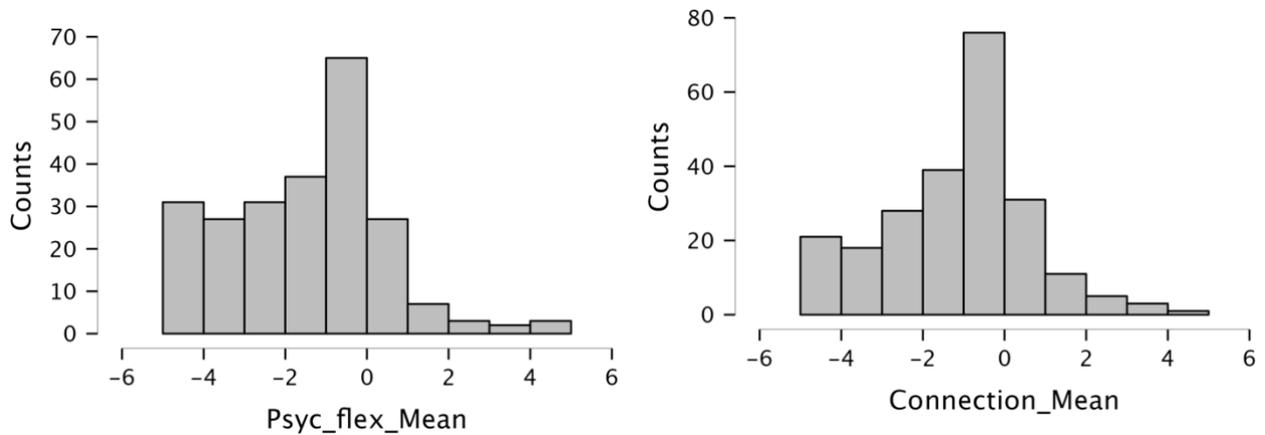
N = 233	Mean	95% Confidence Interval	Frequency (Percentage) of participants reporting perceived improvement	Frequency (percentage) of participants reporting no perceived change	Frequency (Percentage) of participants reporting perceived deterioration
<b>Psychological Flexibility (AQ10)</b>	-1.41	[-1.66, -1.16]	161 (69.10%)	30 (12.88%)	42 (18.03%)
<b>Social Connectedness (SCS)</b>	-1.05	[-1.31, -0.79]	151 (64.81%)	31 (13.30%)	51 (21.89%)

Mean scores range from -5 to 5 with 95% confidence intervals that are below (and do not cross) zero suggesting a perceived reduction, confidence intervals that are above (and do not cross) zero suggesting a perceived increase and zero suggesting no change. Lower numbers suggest bigger reductions.

Frequency of participants reporting perceived improvement shows the frequency and percentage of participants reporting improvement rather than no change or worsening of symptoms. Frequency of participants reporting perceived deterioration shows the frequency and percentage of participants reporting deterioration rather than no change or improvement in symptoms. Frequency of participants reporting no perceived change shows the frequency and percentage of participants reporting no change rather than improvement or worsening of symptoms.

**Figure 2.3**

*Histograms showing distribution density for perceived change in Psychological Flexibility and Connection*



Both unadjusted and adjusted linear regressions show that increases in both psychological flexibility and social connectedness predict perceived change in mental health (DASS total, DASS depression, DASS anxiety, DASS stress and SPIN). All results remained significant ( $p < 0.001$ ) when controlling for demographics age, gender. Table 2.9 presents both unadjusted and adjusted regression coefficients.

**Table 2.9**

N = 233	Unadjusted				Adjusted for age and gender					
	B	95% CI	$\beta$	P	R2	B	95% CI	$\beta$	p	R2
<b>Psychological Flexibility (AQ10)</b>										
DASS Total	1.43	[1.25, 1.61]	0.72	< .001	0.52	1.41	[1.23, 1.58]	0.72	< .001	0.53
DASS Depression	0.61	[0.53, 0.70]	0.62	< .001	0.45	0.60	[0.51, 0.69]	0.66	< .001	0.47
DASS Anxiety	0.31	[0.27, 0.36]	0.64	< .001	0.41	0.31	[0.26, 0.36]	0.64	< .001	0.42
DASS Stress	0.50	[0.43, 0.57]	0.66	< .001	0.44	0.50	[0.42, 0.57]	0.66	< .001	0.44
SPIN Total	1.05	[0.87, 1.23]	0.59	< .001	0.35	1.06	[0.88, 1.24]	0.60	< .001	0.37
<b>Social Connectedness (SCS)</b>										
DASS Total	1.22	[0.94, 1.31]	0.62	< .001	0.38	1.10	[0.92, 1.29]	0.61	< .001	0.40
DASS Depression	0.53	[0.43, 0.60]	0.61	< .001	0.38	0.50	[0.42, 0.59]	0.60	< .001	0.40
DASS Anxiety	0.24	[0.19, 0.29]	0.54	< .001	0.29	0.24	[0.19, 0.29]	0.53	< .001	0.30

DASS Stress	0.36	[0.29, 0.44]	0.53	< .001	0.28	0.36	[0.28, 0.44]	0.52	< .001	0.28
SPIN Total	0.86	[0.68, 1.04]	0.53	< .001	0.28	0.86	[0.68, 1.04]	0.53	< .001	0.29

*Unadjusted and Adjusted Regressions for Predicting Perceived Change in mental health*

DASS = Depression, Anxiety and Stress Scale

SPIN = Social Anxiety Inventory

Adjusted model includes age and gender.

## Discussion

This exploratory study is, to my knowledge, the first to look at retrospective perceived change in mental health after use of a classic psychedelic in an autistic population. It sought to investigate three things. Firstly, whether autistic people report perceived changes in mental health which they attribute to psychedelic use. Secondly, if any perceived changes are associated with the quality of the experience (how mystical and challenging it is) or the context of experience (the supportiveness of the context and a person's mindset before taking psychedelics). Thirdly if any changes in mental health are related to changes in social connectedness or psychological flexibility. The study found that on average, participants reported perceived improvement in all areas of mental health and that this was predicted by the degree of mystical experience with more mystical experiences predicting more perceived improvements in mental health. Perceived increases in social connectedness and perceived change in psychological flexibility also predicted perceived improvements in mental health.

On average, participants reported perceived improvements in symptoms of mental health problems attributed to their most impactful psychedelic experience. This was the case for each of the measures of perceived change in mental health; the adapted DASS total, its three subscales (the adapted DASS depression, DASS anxiety and DASS stress) along with the measure of Social Anxiety (the adapted SPIN). This fits with previous data in non-autistic populations, a review of clinical trials of psychedelic-assisted psychotherapy for mental health conditions found that psychedelics significantly reduced clinical outcomes associated with anxiety, depression, PTSD, OCD and substance use disorders (Wheeler & Dyer, 2020).

Participants reported bigger perceived improvements in symptoms of depression (an average reduction of -1.71 out of maximum possible of -5) compared with smaller perceived improvements in anxiety, stress and social anxiety (-0.53, -1.10 and -0.98 respectively). This

fits with previous evidence from the small number of clinical trials which have been carried out in non-autistic populations which all showed an improvement in symptoms of treatment resistant depression following psychedelic use (Carhart-Harris et al., 2016, 2018, Griffiths et al 2016, Osorio et al., 2015). A review of these studies found psychedelics were not only effective in treating depressive symptoms but were also fast, with significant differences observed from day one, much faster than with serotonergic anti-depressants (Romeo et al, 2020). Results from this study suggest that similarly to with non-autistic people, psychedelics may be associated with improvements in symptoms of depression in autistic people. This suggests a potential rationale for including autistic people in future psychedelic trials to find out if the perceived improvements reported by participants in this study are replicated in controlled studies.

The study supports previous literature suggesting a therapeutic role of psychedelic-induced mystical experiences (e.g. Haijen et al, 2018 & Roseman et al, 2018). Reported degree of mystical experience significantly predicted perceived change on all mental health outcome measures (adapted DASS total, DASS depression, DASS anxiety, DASS stress and SPIN) explaining 12.4% of variance. This suggests that similarly to with non-autistic people, the degree of mystical experience is an important predictor of therapeutic outcome.

One hypothesis as to why mystical experiences predict therapeutic outcome is that it is the combination of a mystical and therefore impactful psychedelic experience alongside psychedelic's ability to effectively drive neuroplasticity in relevant circuits which is important in driving change in mental health (Artin et al, 2021).

Mystical experiences involve thought, mood, and perceptual changes and extreme changes in subjective experience (Griffiths et al., 2006). The Cognitive Behavioural model of depression (Beck & Alford, 2009) suggests that depression is maintained by getting stuck in a cycle of negative thinking, feeling and behaving. Mystical experiences involving changing thoughts, moods and perception helps bring in flexibility in thinking. Studies suggest the improved psychological flexibility and personal meaningfulness associated with mystical experiences help people experiencing depression or anxiety to reframe how they view their lives, their relationships with others etc (Davis et al, 2020 & Watts et al, 2017).

The combination of a mystical experience and neuroplasticity could provide a unique way of rapidly consolidating effects of the experience from long-term retention. This is hypothesised to work in a similar way to trauma, where a single very intense experience,

linked to plasticity causes long term (in this case detrimental) effects on mental health (Mahan & Ressler, 2012).

Factors other than the degree of mysticalness which were hypothesised to predict perceived change in mental health (how ‘challenging’ the experience was, the setting and set) did not significantly predict change in depression, anxiety and social anxiety when controlling for demographic factors and their covariates. The results fit with previous research on non-autistic populations which found that the challengingness of the experience did not significantly predict subsequent changes in wellbeing (Haijen et al, 2018).

It is important to note that not all participants reported perceived improvements in depression, anxiety, stress and social anxiety, some reported no changes and some reported a worsening of symptoms. This was most pronounced for the Anxiety subscale of the DASS where 42/233 (18.03%) of participants reported noticing no changes and 47/233 (20.17%) reported worsened anxiety after their chosen psychedelic experience (see table 5 for full statistics). It is important to take into account potential negative outcomes when considering potential clinical applications of psychedelics. Because previous psychedelic trials do not always measure change in anxiety it is difficult to compare this finding to non-autistic populations. It could be the case that in an autistic population, where rates of anxiety are higher than a non-autistic population (Hollocks et al, 2019 & Lai et al, 2019), the risk of a person experiencing worsening symptoms of anxiety is higher. This highlights the importance of looking at change in anxiety in future research.

As suggested by previous research changes in mental health were significantly associated with both perceived changes in psychological flexibility and perceived changes in social connectedness. This was the case for overall perceived change in mental health (overall DASS) along with perceived change in depression, anxiety, stress and social anxiety (measured by DASS depression, DASS anxiety, DASS stress and SPIN). For overall mental health (total DASS scores) variance explained by perceived change in psychological flexibility was 52% suggesting a strong association between the two. This fits with previous research in non-autistic (Davis et al, 2020) and autistic (Pahnke et al, 2019) populations suggesting an increase in psychological flexibility is associated with improvements in mental health. Similarly for overall mental health (total DASS scores) variance explained by

perceived change in social connectedness was 38% suggesting a strong association between the two. This fits with previous research showing that improved connectedness was a key part of recovery for mental illness (Leamy et al, 2011). This supports the hypothesis that perceived therapeutic improvement attributed to psychedelics is linked to improvements in psychological flexibility and social connectedness. Future experimental studies could be used to test these hypotheses.

### **Strengths and Limitations**

The study's retrospective, cross-sectional design carries some limitations and results should be considered in this context. The study relies on participants being able to accurately remember experiences that often took place many years previously (Mean = 3.99 years ago SD = 6.39) and be able to accurately attribute changes in mental health to these drug experiences. It also relies on participants being able to accurately name the drugs they used (in many of the countries where participants are from psychedelic drugs are controlled substances meaning participants may not have accurate information about the active ingredients).

Due to the design of the survey there was limited control over covarying variables. Steps were taken to improve this such as measuring potential covariants identified in previous literature and controlling for these in linear regression models. Due to the cross-sectional nature of the design causality cannot be established.

A further limitation relates to how participants were recruited. Participants who responded to advertisements shared by organisations such as the Autistic Psychedelic Community may have contributed to bias within the sample with followers of these organisations more likely to have experienced positive outcomes from psychedelics.

### ***Sample and Generalisability***

Due to the resource intensive nature of conducting psychedelic trials, sample sizes tend to be very small. One advantage of using a cross-sectional, retrospective design is that it meant a larger sample size could be obtained. The sample is varied in terms of age (ages ranged between 18 and 67) and gender (in this sample 48.5% of participants identify as men,

with 23.61% identifying as women and the rest identifying as non-binary, trans or other). In autistic samples men are often over-represented. This could be because men are more likely to be diagnosed with autism, the average male to female odds ratio for people diagnosed with autism is 4.56 compares to estimates that look at non- diagnosed autism traits of 3.25 (Loomes et al., 2017). The large representation (27.89%) of people who do not identify within the binary of man or woman is something commonly seen within an autistic population, for example a largescale cross-sectional review found that gender diverse people were more likely to be diagnosed with autism and had more autistic traits than in the general population (Warrier et al., 2020). This suggests the study represents the gender diversity within the autistic population.

The sample is predominantly white (83.26%) with the majority (97.42%) of participants coming from Western countries such as United States, United Kingdom, Mainland Europe, Canada and Australia. Therefore the study represents a Western sample and results cannot be generalised to people who live in other places. 58.37% of the sample were University educated, around double what would be expected in the general population of the UK suggested a particularly educated sample (Mayhew & Deer., 2007).

### **Scientific and Clinical Implications**

Although widely used treatments for depression such as anti-depressant medication and Cognitive Behavioural Therapy (CBT) have been shown to be efficacious in treating depression a significant number of people do not respond to these treatments (e.g. Lieberman et al., 2005 and Santoft et al., 2019). For autistic people especially the evidence for the effectiveness of psychosocial treatments such as CBT show mixed results (e.g. review by Menezes et al., 2020).

Results from this study suggest support a rationale for further research into the therapeutic potential of classic psychedelics for autistic people. Small, open label studies looking at safety, tolerability and efficiency of psychedelics such as the one completed by Carhart-Harris et al (2016) may be the next step toward controlled trials. Longitudinal survey designs which compare measures before and after a psychedelic experience could also be

used to gather evidence in a naturalistic settings to negate the issue of recall bias whilst maintaining a large sample size.

The results may also give an insight into why autistic people may use Psychedelic drugs. This could inform policy decisions around control and use of these drugs as therapeutic agents.

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### **Part 3: Critical Appraisal**

## **Introduction**

In this critical appraisal I discuss the challenges and dilemmas I faced when designing, analysing and writing up the findings from my empirical paper. I start by reflecting on how I came to study this topic. I include some reflections on my context in relation to the topic of psychedelics and autism research and how this may have impacted the empirical study. Secondly, I talk about some of the challenges I faced in designing the study and collecting and analysing the data and how I overcame these challenges. Thirdly I discuss some of the limitations of the study. Fourthly I discuss some of the ethical dilemmas and questions I faced and how I managed these. I finish by summing up my experiences and key learnings.

### **Reflections on subject choice and my context**

#### **Subject choice**

I was attracted to the topics of psychedelics and autism for several reasons. Firstly, at the time when I was considering the topic of my thesis I was on a placement working with children with autism. I had enjoyed learning about autism and speaking to young people about their experiences. My interest in psychedelics developed from my own experiences of taking psychedelics when I was younger and the impact that these experiences had on me. For example, I feel like I gained a new found sense of connection to nature as well as a reduction in concerns about what other people thought about me. These experiences motivated me to find out more about psychedelics and especially their therapeutic potential, given the benefits I had experienced. My interest in the combination of autism and psychedelics initially came from reading and listening to autistic people's descriptions of their experiences of using psychedelics and the lasting impact of these experiences. I was

especially moved by a book by the Autistic Psychedelic Community (2021) in which autistic people shared their stories and experiences and discussed the impact of using psychedelics.

Given that I am someone with personal experience of using psychedelics I was aware that I am not coming to the research question without bias – I already held a belief about the potential benefits of psychedelics. As a researcher it is important to be objective and therefore it was important for me to acknowledge this potential bias and to keep this in mind throughout all stages of my research from design to write up. I was also aware of the enthusiasm within the psychedelics field as to the therapeutic potential of psychedelics and wanted to make sure I remained rooted in the science rather than in the hype. Reviewing the literature into lasting effects of psychedelics for the literature review (part 1 of the thesis) helped me to look critically at the literature and gave me an awareness of the methodological problems associated with a lot of psychedelic research (e.g. low sample sizes, lack of control groups). I also found it helpful to read literature on negative experiences of psychedelics to remind myself of the diversity of experience and that my experiences were not universal.

### **Studying Autism**

I am not autistic. Because autism is something I have no lived experience of I felt it was especially important to try and hold in mind the perspectives of autistic people when carrying out the research. This would ensure that the study would be sensitive to the way autistic people wanted to be talked about in research and to ensure that our results would be as impactful as possible. One of the ways we achieved this was by asking not only about participants' experiences by using measures but also by using open response fields where participants could describe their experiences in their own words. Although the analysis of these responses is beyond the scope of this thesis there is a plan for a future trainee to analyse and hopefully publish these in the future. We also looked at a UK survey asking autistic

people which language they preferred and used language based on this survey (Kenny et al, 2015). We also set out to collaborate with someone from the Autistic Psychedelic Community who has first hand experience of autism and using psychedelics at the design and recruitment phase. We reached out to [REDACTED] who helped us frame our research questions in an inclusive way. [REDACTED] also helped the survey reach a much larger audience than we could have achieved without their support and help with dissemination. This reinforced the importance of the inclusive practice that I had been discussing throughout the DClinPsy in reflective groups and in lectures. Inclusive research design leads to better results by increasing buy in from subject communities and helps support the community being researched.

### **Previous experiences of research**

Before this project my research experience was limited. Other than my undergraduate and master's degrees I had no prior experience of conducting or writing up research. This meant I came to the project with a lack of confidence and without a clear idea of what the process of working on such a considerable piece of research would entail and how challenging it might be. At the outset of the research project I struggled with feelings of low self esteem and found myself comparing my own skills unfavourably with other members of my DClinPsy cohort. I felt comparatively inexperienced and feared that my research would not be valued as highly as others'. In hindsight I believe I undervalued my previous experiences and expertise as I found the process manageable and generally enjoyable. Hopefully in the future I can be more confident in my research skills which will enable me to develop my ideas further and seek out discussions with other researchers.

One area in particular where I felt I lacked confidence was in statistical analysis. In order to analyse the data from my study I needed to use linear regression models, a statistical

technique I had no experience with (other than approaching this technique theoretically during lectures). Because I lacked confidence using these methods I found myself putting off my statistical analysis. When I sat down to do my statistical analysis I found I was getting easily stuck and frustrated when things went wrong because I did not understand why they went wrong and what I needed to change. This meant I spent a lot of time reading and learning to try and work out what I needed to do differently. If I encountered this problem again I would take a different approach. I would make sure to enlist the help of colleagues with a good understanding much earlier in the process. I would also spend more time looking at studies which used similar analyses to get a feel for how they presented and discuss their results.

## **Challenges**

### **Designing the study**

The first challenge I encountered was how best to design the study. I knew that I wanted to look at the effects of psychedelics on mental health in autistic people but did not know how exactly I would frame my research question or which study design would best answer it. Due to the time limit (2 years) and financial limitations, given that we had no budget for research, I had to think carefully about what kind of research would be both practical, given the constraints, and still able to make a valuable contribution to the field. There is currently no academic literature looking directly at autistic people's experiences of using psychedelics, so we wanted our study to be an exploratory study. We decided that a good starting place was to use a cross sectional design asking people who have already used psychedelics whether they attributed any perceived changes in their mental health to a psychedelic experience. Depending on findings this could form a useful basis and rationale for future experimental studies or trials. It was difficult to decide between using quantitative

and qualitative methodology: both would be a good starting point when researching a new area. I decided to use quantitative methodology, this was partly because the methodology suited the question and allowed me to look at the association between predictor and outcome variables I was interested in. Even though I lacked confidence, I also wanted to challenge myself to use statistical analysis. Looking at and critiquing previous research in non-autistic populations helped me to finalise the design, which I based on a study by Davis et al (2020). It was important to clearly define my research questions. I spent time reviewing related literature to decide which potential covariates and predictor variables were important to include and how to appropriately to measure these. I also thought about how the covariates and measures I used relate to my target population, for example finding out more about the link between autism and mental health.

The second challenge came from designing the materials for the study. This involved developing a new survey to answer me and my thesis partner's different but related research questions. This was challenging as it involved balancing different requirements; covering everything necessary to sufficiently answer me and my partner's research questions whilst still being appropriate and accessible for participants. To make sure that it was feasible for participants to finish the survey it was important that the survey did not take prohibitively long to complete meaning we had to make decisions about what could and could not be included. I first made sure to include measures of the variables related to my research questions measured by (where possible) validated measures that have been used with autistic participants. I then decided which covariables to include based on which were most referred to in the literature. I also including demographic questions to enable a description of the sample. Finally, I spent time talking to my thesis partner and supervisors to get second opinions on whether anything important had been missed. To ensure the survey was not too long I timed how long it took to complete the survey by asking a few volunteers to fill it out.

In hindsight it would have been helpful to do this with a few autistic volunteers to make sure that the estimates for the timings were the same.

If I were to do a similar research project in the future, I would spend more time streamlining the survey to include only the essential measures or looking for shorter measures. For every submitted response we received around three unsubmitted response (that could not be used) suggesting that people had given up on the survey before completing.

### **Adaptations for autistic participants**

In order to make sure the questionnaire was appropriate for autistic people we incorporated guidance on making surveys accessible for autistic people (Nicolaidis et al, 2020) such as substituting difficult vocabulary words, simplifying sentence structure and adding explanatory prefaces. This was done whilst also trying to keep measures as close to their previously validated form as possible. Where possible we used measures which had previously been used with autistic participants. We also asked our autistic co-contributor to check through the survey to check for comprehensibility. Our co-contributor talked about how in autism people can understand and relate differently to their emotions. This could impact how participants answer questions, especially questions which specifically ask about perceived change in feelings.

If I was to do the survey again I think it would be important to have multiple autistic people check the survey and to check that their understanding of the questions (especially questions around emotions) matches with our understanding of the questions being asked.

### **Recruitment**

Another challenge we faced was how best to recruit participants. Because of the inclusion criteria (participants have to be autistic and have used a psychedelic drug) this

meant the majority of people would not be suitable participants. To access our target population we needed to make sure adverts for the survey were displayed in places where our target audience might see. We used social media sites such as facebook and twitter to share our advert. Shares on these sites did not yield many participants and it was very time intensive to find people who could share the advert and had an audience that fitted our inclusion criteria. We also targeted specific forums on reddit (for example forums for autistic people or people who have experience of using psychedelics) which was also very time consuming. Despite putting lots of time into sharing our adverts and asking other people to share adverts we still struggled to recruit. One of the best things we did to improve recruitment was to enlist the help of the Autistic Psychedelic Community, an organisation who already have ties with our target demographic and asking them to share the advert through their mailing list and website. Meeting with Aaron, their founder, he also gave us ideas about where best to post to increase recruitment.

### **Working with another person**

This thesis was part of a joint project with another trainee where we both used the same or similar data to answer a different research question. There were many positives from working with another person on the project. For example, we were able to share the workload for ethics application, survey building, recruitment and data cleaning. It was also helpful to have someone else who was familiar with the literature and methodology to share ideas with and discuss dilemmas. There were also some challenges. It was difficult to split the project in a way that felt both fair and made sense conceptually.

### **Challenges in psychedelic research**

Some of the challenges I faced in designing and conducting this research reflect the difficulties faced in psychedelic research generally. Due to the legal status of psychedelics, studies where these drugs are administered are expensive and can be practically difficult to do (Curren et al, 2018). This means the designs such as the one I used, where we ask people about previous psychedelics are the only thing possible within the time constraints of a DCLinPsy thesis.

## **Limitations of the Study**

### **Limitations linked to the design**

One of the main limitations of the study (which is also written about briefly in the discussion section) comes from the design, where a survey was used to ask participants to retrospectively rate how much they attribute perceived changes in mental health to a selected psychedelic experience. This relies on both the ability to accurately remember changes in mental health but also to accurately attribute these changes to the selected experience. Participants may mis-remember. They may also be influenced by expectations of change, for example a pre-existing belief that psychedelics improve mental health may bias answers. Autistic people are more likely to experience alexithymia (problems with identifying or articulating their own emotions) (Berthoz & Hill, 2005), potentially impacting their ability to accurately report changes in mental health.

There are however also benefits of taking this approach. We are getting a measure of someone's subjective experience of change. This is important when we think about mental health, if people think their symptoms have improved this can be seen as positive, regardless of whether they objectively have experienced change. For example if someone feels like they are experiencing less fear even there was no change by some other metric this could

constitute a positive change. Our survey measures their experience rather than looking at symptoms change based on comparing pre and post measures.

Another possible limitation of this study relates to the way we obtained the sample. It is possible that participants may have been more likely to take part if they had noticed positive change following psychedelic use. For example, they may have been more motivated to spend time filling in a survey related to an experience which they believe was important and linked to a big change rather than an experience which felt less significant. This could be true for both positive and negative changes.

### **Limitations linking to possible cofounders (multiple experiences)**

One of the dilemmas we faced when designing the study was how to measure change from a specific experience when participants likely had multiple experiences of using psychedelic drugs. One idea was to exclude participants who had used psychedelics more than once. However, due to the already small pool of potential participants and the fact that people often use psychedelics more than once, especially if they've found them helpful, this approach did not make sense. Instead, we decided to ask participants to select a 'most impactful' experience and instead to answer questions based on that experience only.

## **Ethical dilemmas**

### **Psychedelics as a harmful drug**

As psychedelics have the potential to cause harm it is important that we do not promote or encourage psychedelic use. We made sure to make this clear in our introduction sheet and included information on how to get support for problematic drug use.

### **The impact of filling out the survey**

Because our survey asked some questions about potentially upsetting topics (for example asking participants about their mental health) there was a concern about the potential psychological impact to participants of completing the survey. To reduce the potential for harm we made sure that we made it clear that these questions would be asked on the information sheet so participants could make an informed decision about whether they wanted to take part. We also had a page which described how support could be obtained around mental health (see appendix \_)

### **Data protection**

When designing our survey we had to balance getting the data we needed to answer our research question and to describe the sample with participants' rights to confidentiality. We were keen that our data be available for analysis by other researchers in order to have complete transparency and to allow for as many scientific findings as possible to come from our data. However, for this to be possible it meant we had to be careful about what demographic data we used as there may be a small chance it would be possible to identify participants through their demographic data. To manage this we decided to present data categorically rather than specifically (for example age 18 – 25 rather than specific ages).

### **Psychedelics as a 'treatment' for mental health problems**

Another ethical dilemma I encountered was around how psychedelics fit with my understanding of mental health. As a Clinical Psychologist I use multiple models to formulate and understand distress including looking at a person's social context alongside looking at biological and psychological factors (such as thoughts, feelings and behaviours). Psychedelic interventions intervene at a biological level suggesting a problem very much located in the person and their biology. Focussing on psychedelics as a potential 'cure' for mental health

problems could minimise the effect that social factors have. This is especially important for autistic people where social factors such as discrimination, a lack of appropriate adaptations and bullying can have a negative impact on autistic people's mental health (Fuld, 2018).

However I do not see psychedelics' mechanism of action as purely biological. My findings together with past literature suggest that a sense of connection, new and mystical experiences and increasing prosocial behaviour are associated with psychedelic use. The impact of psychedelics on perceived change tells us something interesting about the therapeutic impact of the drug and also about the therapeutic impact of experiences that are associated with psychedelics, such as social connectedness and psychological flexibility (e.g. Carhatt-Harris et al, 2018 & Davis et al, 2020).

### **Conclusion**

Overall this project has taught me the importance of using my reflective skills to consider how my own context and experiences might effect my research and the importance of maintaining a cautious and critical approach to research design. A theme I have kept coming back to has been the importance of asking for help and collaborating with people who have expertise I lack (for example speaking to a statistics expert or experts by experience from the participant group). I have found the project thought provoking and have enjoyed having the opportunity to contribute to a novel and exciting area of research.

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## Appendix

### Appendix 1: Ethical Approval Letter

UCL RESEARCH ETHICS COMMITTEE  
OFFICE FOR THE VICE PROVOST RESEARCH



17<sup>th</sup> August 2021

Professor Sunjeev Kamboj  
Research Department of Clinical, Educational and Health Psychology  
UCL

Cc: Charlotte Rice & Jack Stroud

Dear Professor Kamboj

**Notification of Ethics Approval with Provisos**

**Project ID/Title: 20251/001: Autism and Psychedelics: Autism and Psychedelics: exploring the experiences of psychedelic use in autistic people**

Further to your satisfactory responses to the Committee's comments, I am pleased to confirm in my capacity as Chair of the UCL Research Ethics Committee (REC) that your study has been ethically approved by the UCL REC until **1<sup>st</sup> December 2023**.

Ethical approval is subject to the following conditions:

**Notification of Amendments to the Research**

You must seek Chair's approval for proposed amendments (to include extensions to the duration of the project) to the research for which this approval has been given. Each research project is reviewed separately and if there are significant changes to the research protocol you should seek confirmation of continued ethical approval by completing an 'Amendment Approval Request Form' <http://ethics.grad.ucl.ac.uk/responsibilities.php>

**Adverse Event Reporting – Serious and Non-Serious**

It is your responsibility to report to the Committee any unanticipated problems or adverse events involving risks to participants or others. The Ethics Committee should be notified of all serious adverse events via the Ethics Committee Administrator (██████████) immediately the incident occurs. Where the adverse incident is unexpected and serious, the Joint Chairs will decide whether the study should be terminated pending the opinion of an independent expert. For non-serious adverse events the Joint Chairs of the Ethics Committee should again be notified via the Ethics Committee Administrator within ten days of the incident occurring and provide a full written report that should include any amendments to the participant information sheet and study protocol.

The Joint Chairs will confirm that the incident is non-serious and report to the Committee at the next meeting. The final view of the Committee will be communicated to you.

██  
University College London  
Tel: ██████████  
<http://ethics.grad.ucl.ac.uk/>

**Final Report**

At the end of the data collection element of your research we ask that you submit a very brief report (1-2 paragraphs will suffice) which includes in particular issues relating to the ethical implications of the research

i.e. issues obtaining consent, participants withdrawing from the research, confidentiality, protection of participants from physical and mental harm etc.

In addition, please:

- ensure that you follow all relevant guidance as laid out in UCL's Code of Conduct for Research: <https://www.ucl.ac.uk/srs/file/579>
- note that you are required to adhere to all research data/records management and storage procedures agreed as part of your application. This will be expected even after completion of the study.

With best wishes for the research.

Yours sincerely

A black rectangular redaction box covering the signature of Professor Lynn Ang.

**Professor Lynn Ang**  
**Joint Chair, UCL Research Ethics Committee**

## **Appendix 2 – Outline of joint work**

The empirical paper was completed as part of a wider project exploring the perceived changes attributed to psychedelic use in an autistic population. The current thesis was completed as part of a joint project with Jack Stroud.

The project was split as follows:

- The outcome measures used were different. My thesis focussed on perceived changes in mental health (depression, anxiety, stress and social anxiety) and perceived changes transdiagnostic predictors of mental health (psychological flexibility and social connectedness). Jack's thesis focused on perceived change in autism specific factors (features of autism, social functioning and camouflaging). He also looked at the relationship between the context of the psychedelics experience (e.g. where the drug was taken, what mindset the person was in) and the quality of the experience (how mystical and challenging the experience was).
- We worked together on the ethics application, the design and building of the survey, participant recruitment and data cleaning.
- All data analysis and write up was done separately.

## Appendix 3 – Information Sheet and Consent Form

RESEARCH DEPARTMENT OF CLINICAL, EDUCATIONAL AND HEALTH  
PSYCHOLOGY

Participant Information Sheet

UCL Research Ethics Committee Approval ID Number: 20251/001

PLEASE SAVE A COPY OF THIS INFORMATION SHEET

Title of Study: Autism and Psychedelics: exploring the experiences of psychedelic use in autistic people.

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Department: UCL Department of Clinical, Educational and Health Psychology

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Name and Contact Details of the Researcher(s): Jack Stroud [REDACTED] Charlotte Rice  
[REDACTED]

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Name and Contact Details of the Principal Researcher: Prof. Sunjeev Kamboj (email:  
[REDACTED])

### 1. Invitation Paragraph

You are being invited to take part in a research project which is being conducted by University College London (UCL) as part of the researchers' doctoral thesis. Before you decide to continue, it is important that you understand why it's being done and what taking part will involve. Please take some time to read the following information carefully and discuss it with others if you wish. Please contact us using the above email addresses if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part, and be aware that your participation is completely voluntary.

### 2. What is the project's purpose?

The current study aims to further our understanding of the experiences of autistic people who have used psychedelic drugs.

### 3. Why have I been chosen?

To take part you must be at least 18 years old, have a good understanding of the English language, have been given a diagnosis of autism by a healthcare professional and/or self-identify as autistic, and have used any classic psychedelic (for example, LSD or LSD derivatives, 'acid' (e.g. 1P-LSD, 1CP-LSD), Ayahuasca, DMT, 5-MeO DMT, Mescaline (Peyote, San Pedro), Magic mushrooms (psilocybin)), MDMA or ketamine at least once.

### 4. Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be asked to electronically give consent which confirms for us that you agree to take part in the

study and understand what this means. You can withdraw from the study, at any time without giving a reason. If you are a UCL student please do not feel under any obligation from UCL staff to participate.

5. What will happen to me if I take part?

This study requires you to fill out a one-off pseudonymous online survey that takes approximately 30 minutes to complete. The survey asks you to answer questions about your background, autism, mental health and psychedelic drug use. It then asks about how you think the psychedelic experiences have impacted your life, autism and mental health. You can withdraw from the study at any point during the survey by simply closing the browser. For example you will be asked questions like, ‘during your psychedelic use did you experience loss of time and space’ and ‘please describe any changes in your mental health that you attribute to the selected psychedelic experience’.

We are aware that psychedelic experiences can be incredibly varied and are interested in hearing both positive and negative experiences, or anything in between. We do not advocate or endorse the use of psychedelics or any other illegal drugs, which can have harmful health, social and occupational consequences. If you would like advice on how to access support for reducing problematic drug use, please follow this link: [Link to sources of support document, see appendices].

6. What are the possible disadvantages and risks of taking part?

Please be aware we will be asking questions about psychedelic experiences, mental health and historical drug use and that some people may find answering these distressing. As this is an online survey we are unable to provide support to people who are experiencing current mental health difficulties. If you would like to find out more about mental health and how to seek support please follow this link: [Link to sources of support document, see appendices]. You can exit the survey at any time. We appreciate the time you dedicate to this project.

7. What are the possible benefits of taking part?

Whilst there are no immediate benefits for those people participating in the project, it is hoped that you will leave with the knowledge that you have contributed in some of the following ways:

Autistic people are often overlooked in psychedelic research and we hope this research will contribute to understanding this under-researched area

- You inform the scientific community about autistic people’s experiences of psychedelics and their impact
- Your personal experience helps shape better theories about the relationship between psychedelic drug use, autism and well-being in autistic people
- The project has the potential to inform the development of future studies looking at wellbeing in autistic people

8. What if something goes wrong?

If you wish to raise a complaint then please contact Professor Sunjeev Kamboj (the Co-Principal Investigator for the study) at [REDACTED], or Professor Will Mandy (the Co-Principal Investigator for the study) at [REDACTED]. If you feel that your complaint has not been handled to your satisfaction, you can contact the Chair of the UCL Research Ethics Committee at [REDACTED].

9. Will my taking part in this project be kept confidential?

The data you provide is very valuable to us. The data we will be collecting is considered pseudonymous. This is because although we will not collect data which could directly identify you (such as your IP address or date of birth) we will be collecting demographic data such as (age, ethnicity) which if collated could present a small risk of identification. To prevent identification through collation of demographic data we will only publish demographic information online in broad categories (for example age in 10 year bands). All data will be stored on the secure UCL network.

Due to the fact no directly identifying information is collected it is not possible to remove your responses once submitted, as we would be unable to identify which response was yours. So by submitting your completed survey you are consenting to take part in the study. If you do not complete the survey and then close the webpage, this will be considered as a withdrawal of consent and this data will be deleted prior to analysis.

The survey includes some open questions about your experiences where you can respond in free-text boxes. Please do not include any identifying information such as names, places, physical appearance etc. We will screen these responses for any potentially identifying information and delete this prior to analysis, data sharing and publication. The publication of study results will not include any data that can identify you. Brief, fully anonymised, quotes will be used in disseminated reports. You do not have to fill in these free-text boxes.

The data we collect from this study will help to advance the scientific understanding of autistic people's experiences of psychedelic drug use. To improve the transparency of scientific research on autism and psychedelics, we will make the pseudonymised data we collect in this study freely available online. Data in the form of numerical values from questionnaires will be made openly available so other researchers can confirm our statistical analyses. In addition, the fully anonymised free-text responses, following screening to ensure removal of any identifying information, will also be made freely available online. The findings of the study will be published in publicly available doctoral dissertations which will be available online approximately 18 months after data collection.

10. Limits to confidentiality

Confidentiality will be respected unless there are compelling and legitimate reasons to believe that you or someone is in serious danger or at risk of imminent harm. In such cases the University may be obliged to contact relevant statutory bodies/agencies.

11. What will happen to the results of the research project?

The results will be presented as scientific papers in peer reviewed journals, at conferences, and in student dissertations. You will not be able to be identified in any reports, publications, talks or media. The findings will be published on the UCL Clinical Psychopharmacology Unit's website.

The data we collect from this study will help to advance the scientific understanding of autistic people's experiences of psychedelic drug use. To improve the transparency of scientific research on autism and psychedelics, we will make the fully anonymous data we collect in this study freely available online. Data in the form of numerical values from questionnaires will be made openly available so other researchers can confirm our statistical analyses. In addition, the fully anonymised free-text responses, following screening to ensure removal of any identifying information, will also be made freely available online. The findings of the study will be published in publicly available doctoral dissertations which will be available online approximately 18 months after data collection.

## 12. Local Data Protection Privacy Notice

Notice:

The data controller for this project will be University College London (UCL). The UCL Data Protection Officer provides oversight of UCL activities involving the processing of personal data, and can be contacted at [data-protection@ucl.ac.uk](mailto:data-protection@ucl.ac.uk)

This 'local' privacy notice sets out the information that applies to this particular study.

Further information on how UCL uses participant information can be found in our 'general' privacy notice.

- For the general privacy notice click here [Please see below Participant Information Privacy Notice]

The information that is required to be provided to participants under data protection legislation (GDPR and DPA 2018) is provided across both the 'local' and 'general' privacy notices.

For this study, the categories of personal data collected will be as follows: Gender; Age; Ethnicity; Sexual Orientation or Sex Life; Mental Health and Drug Use information.

Collection of such demographic information is important to our research because it helps us understand whether the respondents are representative of the autistic population as a whole and how people with different demographics might have different experiences. The survey aims to find out about psychedelic use so we need to ask participants about this. We ask about mental health because we know that psychedelic use is associated with changes in mental health and we want to know autistic peoples experiences of mental health after using psychedelics.

The lawful basis for processing your personal data is the performance of a task in the public interest, and for scientific and historical research or statistical purposes. You can provide your consent for the use of your personal data in this project by completing the consent form on the next page.

Your personal data will be processed so long as it is required for the research project. Data will be pseudonymous from point of collection.

If you are concerned about how your personal data is being processed, or if you would like to contact us about your rights, please contact UCL in the first instance at [REDACTED]. To improve the transparency of scientific research on autism and psychedelics, we will make the fully pseudonymous data we collect in this study freely available online. Data in the form of numerical values from questionnaires will be made openly available so other researchers can confirm our statistical analyses.

### 13. Contact for further information

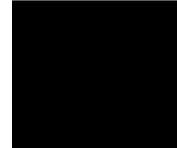
The study is being conducted by researchers from the Department of Clinical, Educational and Health Psychology at University College London.

Jack Stroud

Charlotte Rice

Prof Sunjeev

Prof Will Mandy



If you would like more information or if anything is unclear, please contact the researchers using the contact details above. If you decide to take part, please save a copy of this information sheet as well as your completed consent form (to be completed on the next page). Thank you for considering taking part in this research. If you have any questions arising from the Information Sheet, please contact the researcher to ask them before you decide whether to join in. You are advised to save a copy of this Consent Form to keep and refer to at any time.

I confirm that by ticking the box below I am consenting to take part in this study. I am confirming that I have read and understood the information sheet and that I understand that once I submit the completed survey I will be unable to withdraw my data.

## Appendix 4 – Extra analysis

**Table 1**

*T-tests comparing participants diagnosed with Autism to participants who self-diagnose*

	Professional Diagnosis Group (N=136)		Self-Diagnosis Group (N=97)		DF	t	p
	M	SD	M	SD			
<b>DASS Total</b>	-1.12	1.40	-1.10	1.08	231	-0.13	0.90
<b>DASS Depression</b>	-1.74	1.89	-1.65	1.58	231	-0.41	0.68
<b>DASS Anxiety</b>	-0.56	1.03	-0.50	0.84	231	-0.47	0.64
<b>DASS Stress</b>	-1.06	1.60	-1.15	1.22	231	0.48	0.63
<b>SPIN</b>	-1.12	1.57	-0.78	1.11	231	-1.83	0.07
<b>MEQ</b>	3.20	1.08	3.14	1.22	231	0.39	0.69
<b>AAQ-II</b>	-1.44	2.12	-1.37	1.64	231	-0.29	0.77
<b>SCS</b>	-1.07	1.87	-1.03	1.81	231	-0.16	0.90

DASS – Depression, Anxiety and Stress Scale

SPIN – Social Phobia Inventory

MEQ – Mystical Experiences Questionnaire

AAQ-II – Acceptance and Action Questionnaire

SCS – Social Connectedness Scale

**Table 2**

*Unadjusted and Adjusted Regressions for Predicting Perceived Change on DASS*

*(depression)*

Variable	Unadjusted			Adjusted					
	B	95% CI	$\beta$	p	R2	B	95% CI	$\beta$	p
<b>Predictors</b>									
MEQ	-0.13	[-0.18, -0.09]	-0.36	<.001	0.13	-0.13	[-0.18, -0.08]	-0.36	<.001
CEQ	0.05	[-0.01, 0.10]	0.10	0.12	0.01	0.05	[-0.02, -0.08]	0.10	0.15
Setting	0.26	[-0.22, 0.74]	0.07	0.28	0.01	0.04	[-0.43, 0.52]	0.01	0.85
Set	0.46	[0.14, 0.78]	0.18	<0.01	0.03	0.04	[-0.33, 0.42]	0.02	0.82
<b>Demographics</b>									
Age	0.17	[0.00, 0.34]	0.13	<0.05	0.02	0.17	[0.01, 0.33]	0.13	<0.05
Female (vs Male)	-0.70	[-4.66, 3.27]	-	0.73	-	-0.69	[-4.49, 3.12]	-	0.72
Other (vs Male)	-4.44	[-8.21, -0.66]	-	0.02	-	-3.69	[-7.28, -0.11]	-	<0.05

Note: R2 = 0.18 N = 232

MEQ = Mystical experiences questionnaire

CEQ = Challenging experiences questionnaire

**Table 3**

*Unadjusted and Adjusted Regressions for Predicting Perceived Change on DASS (anxiety)*

	Unadjusted	Adjusted
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Variable	B	95% CI	$\beta$	p	R2	B	95% CI	$\beta$	p
<b>Predictors</b>									
MEQ	-0.06	[-0.08, -0.03]	-0.29	<.001	0.08	-0.05	[-0.08, -0.03]	-0.28	<.001
CEQ	0.03	[-0.01, 0.06]	0.10	0.13	0.01	0.02	[-0.02, 0.05]	0.07	0.34
Setting	0.23	[-0.03, 0.49]	0.11	0.08	0.01	0.11	[-0.15, 0.37]	0.06	0.41
Set	0.23	[0.06, 0.41]	0.17	<0.01	0.03	0.04	[-0.17, 0.24]	0.03	0.74
<b>Demographics</b>									
Age	0.06	[-0.03, 0.16]	0.5	0.19	0.01	0.06	[-0.03, 0.15]	0.09	0.16
Female (vs Male)	-2.00	[-3.99, -0.01]	-	<0.05	-	-0.99	[-3.11, 1.13]	-	0.36
Other (vs Male)	-0.99	[-1.99, 0.02]	-	0.05	-	-1.52	[-3.52, 0.48]	-	0.14

Note: R2 = 0.16 N = 232

MEQ = Mystical experiences questionnaire

CEQ = Challenging experiences questionnaire

**Table 4**

*Unadjusted and Adjusted Regressions for Predicting Perceived Change on DASS (stress)*

Variable	Unadjusted					Adjusted				
	B	95% CI	$\beta$	p	R2	B	95% CI	$\beta$	p	
<b>Predictors</b>										
MEQ	-0.09	[-0.13, -0.05]	0.02	<0.001	0.09	-0.09	[-0.13, -0.05]	-0.30	<.001	
CEQ	0.06	[0.01, 0.11]	0.16	<0.05	0.03	0.06	[0.01, 0.12]	0.16	<0.05	
Setting	0.26	[-0.14, 0.65]	0.09	0.20	0.01	0.07	[-0.33, 0.47]	0.02	0.73	
Set	0.36	[0.10, 0.62]	0.17	<0.01	0.03	0.01	[-0.31, 0.33]	0.00	0.96	
<b>Demographics</b>										
Age	0.02	[-0.12, 0.16]	0.02	0.78	0.00	0.02	[-0.11, 0.16]	0.02	0.73	
Female (vs Male)	-0.25	[-3.52, 3.02]	-	0.88	-	0.01	[-3.21, 3.23]	-	0.99	
Other (vs Male)	-2.31	[-5.42, 0.80]	-	0.14	-	-1.71	[-4.75, 1.33]	-	0.27	

Note: R2 = 0.12 N = 232

MEQ = Mystical experiences questionnaire

CEQ = Challenging experiences questionnaire

**Table 5**

*Unadjusted and Adjusted Regressions for Predicting Perceived Change on Social Phobia Inventory (SPIN)*

Variable	Unadjusted					Adjusted				
	B	95% CI	$\beta$	p	R2	B	95% CI	$\beta$	p	

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<b>Predictors</b>									
<b>MEQ</b>	-0.25	[-0.34, -0.17]	-0.36	<.001	0.13	-0.23	[-0.32, -0.14]	-0.32	<.001
<b>CEQ</b>	0.11	[-0.01, 0.22]	0.12	0.07	0.01	0.06	[-0.07, 0.19]	0.07	0.35
<b>Setting</b>	0.94	[0.01, 1.86]	0.13	<0.05	0.02	0.54	[-0.38, 1.46]	0.08	0.25
<b>Set</b>	1.14	[0.53, 1.75]	0.24	<.001	0.06	0.57	[-0.16, 1.30]	0.12	0.13
<b>Demographics</b>									
<b>Age</b>	0.16	[-0.17, 0.50]	0.06	0.33	0.00	0.17	[-0.14, 0.48]	0.07	0.28
<b>Female (vs Male)</b>	2.88	[-4.85, 10.60]	-	0.46	-	4.68	[-2.70, 12.07]	-	0.21
<b>Other (vs Male)</b>	1.15	[-6.20, 8.50]	-	0.76	-	3.93	[-3.03, 10.89]	-	0.27

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Note: R2 = 0.17 N = 232

MEQ = Mystical experiences questionnaire

CEQ = Challenging experiences questionnaire

## Appendix 5 – Sources of support document

### Mental Health Awareness & How to Access Mental Health and Substance Misuse Services

This information sheet gives suggestions for people living around the work and for people in the UK.

For people living outside of the UK:

If you have concerns about your mental health you should get in touch with your General Medical Practitioner.

If you have immediate concerns about keeping yourself safe please go to your local hospital emergency department and call emergency services.

You can also look at this resource page from the World Health Organisation:

<https://www.who.int/news-room/feature-stories/mental-well-being-resources-for-the-public>

For people living in the UK:

Mental health services are free on the NHS.

In some cases you'll need a referral from your GP to access them.

There are some mental health services that allow people to refer themselves.

#### NHS Online

For local support and information services near you, you can search for:

- Mental health support services

- Drug and alcohol support services

If you have concerns about your mental wellbeing, you'll find lots of tips and advice on dealing with stress, anxiety and depression in the MoodZone at

<https://www.nhs.uk/conditions/stress-anxiety-depression/>

You can also try the mood assessment quiz, which is designed to recommend resources to help you better understand how you feel at <https://www.nhs.uk/conditions/stress-anxiety-depression/mood-self-assessment/>

This quiz uses questions that GPs often use to assess whether someone is anxious or depressed. It also includes links to useful information and advice on mental wellbeing.

You can compare mental health service providers using the services near you search tool.

Enter the name of the mental health service or the service provider and your postcode at <https://www.nhs.uk/service-search>

This includes therapies like cognitive behavioural therapy (CBT) for common problems like stress, anxiety, depression, OCD and phobias. You can refer yourself directly to a psychological therapies service without seeing your GP at [https://www.nhs.uk/service-search/Psychological-therapies-\(IAPT\)/LocationSearch/](https://www.nhs.uk/service-search/Psychological-therapies-(IAPT)/LocationSearch/)

If you have concerns about your drug and alcohol use you can find advice on getting support here at <https://www.nhs.uk/live-well/healthy-body/drug-addiction-getting-help/>

#### Face-to-face

You can also make an appointment with your GP.

A GP will assess your circumstances and offer appropriate advice or treatment. They can also refer you to a psychological therapy service or a specialist mental health service for further advice or treatment.

If you have had thoughts of self-harming or are feeling suicidal, contact someone you can trust immediately, such as a GP or a friend or relative.  
A mental health emergency should be taken as seriously as a medical emergency.

#### In an emergency

Examples of mental health emergencies include thinking you're at risk of taking your own life or seriously harming yourself and needing immediate medical attention.

Call 999 if you or someone you know experiences an acute life-threatening medical or mental health emergency.

You can go to A&E directly if you need immediate help and are worried about your safety.

#### On the phone

You can call NHS 111 if you or someone you know needs urgent care, but it's not life threatening.

For example:

- if you have an existing mental health problem and your symptoms get worse
- if you experience a mental health problem for the first time
- if someone has self-harmed but it does not appear to be life threatening, or they're talking about wanting to self-harm

If you want to talk to someone, the NHS mental health helpline webpage has a list of organisations you can call for immediate assistance at <https://www.nhs.uk/conditions/stress-anxiety-depression/mental-health-helplines/>

These are helplines with specially trained volunteers who'll listen to you, understand what you're going through, and help you through the immediate crisis.

Whether you're concerned about yourself or a loved one, these helplines and support groups can offer expert advice.