SPIRIT Statement: Assessing the Safety, Tolerability, and Feasibility of a Stroboscopic Intervention in Major Depressive Disorder (WP1)

1.

A. TRIAL IDENTIFIER AND REGISTRY NAME

ISRCTN

B. WORLD HEALTH ORGANIZATION TRIAL REGISTRATION DATA SET

NA

2. PROTOCOL VERSION (DATE AND VERSION IDENTIFIER)

Version 1.2 (February 11, 2025)

3. FUNDING

The funding for this project is provided by the Medical Research Council (MRC) through the Developmental Pathway Funding Scheme (DPFS) [APP34051].

4.

A. NAMES, AFFILIATIONS, AND ROLES OF PROTOCOL CONTRIBUTORS

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B. NAME AND CONTACT INFORMATION FOR THE TRIAL SPONSOR

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C. ROLE OF STUDY SPONSOR AND FUNDERS, IF ANY

UoS will ensure regulatory compliance and ethical approval

UKRI funding service supports financial and operational aspects but does not directly influence trial outcomes or interpretation of results.

D. COMPOSITION, ROLES, AND RESPONSIBILITIES OF THE COORDINATING CENTRE, DATA MANAGEMENT TEAM, ET AL

Coordinating centre: Sussex Centre for Consciousness Science (SCCS)

Data management team: Barnett & Bremner will oversee statistical analyses; Schwartzman, Kalus, and Nacker will manage participant data.

INTRODUCTION

This study aims to assess the safety, tolerability, and feasibility of a stroboscopic light intervention for individuals with Major Depressive Disorder (MDD) through two work packages (WPs).

WP1 will conduct an early-phase investigation to systematically evaluate the safety and tolerability of stroboscopic light exposure in individuals with MDD. Participants will undergo 11 short sessions using differing stroboscopic parameters of increasing subjective intensity to determine the parameters that elicit engaging but comfortable experiences.

WP2 will implement a pilot randomised trial testing the feasibility of a 30-minute stroboscopic intervention, administered once per week for four weeks, against a low-experience control condition. Depressive symptoms will be measured before, during, and after treatment to explore potential therapeutic effects using validated measures.

If successful, this study will provide critical preliminary data supporting the future development of a novel, non-pharmacological, accessible, and scalable intervention for depression.

The current protocol describes WP1.

6.

A. DESCRIPTION OF RESEARCH QUESTION AND JUSTIFICATION FOR UNDERTAKING TRIAL

Is stroboscopic light safe, tolerable, and feasible as an intervention for symptoms associated with major depressive disorder (MDD)?

The project's goal is to generate critical preliminary data on the safety, tolerability, and feasibility of a stroboscopic intervention for major depressive disorder (MDD), to support the onward development of the intervention as a safe, accessible, and scalable new approach to alleviating depression.

The project builds on the team's 10+ years of experience conducting neuroscientific research into the perceptual and neural effects of stroboscopic stimulation, and 25 years of clinical experience in treating mood disorders and developing novel interventions for depression. We are not aware of any other ongoing research directed towards establishing clinical and/or therapeutic interventions based on stroboscopic light.

Why stroboscopic light? The most distinctive line of evidence comes from a recent large-scale immersive multisensory experience called Dreamachine, created by an interdisciplinary team with Schwartzman and Seth as the lead scientists. Dreamachine used stroboscopic light and spatial sound to enable nearly 40,000 people to safely experience stroboscopically induced visual hallucinations, delivering an opportunity sample of thousands of reports indicating the positive effects of strobe on mood and mental health, including a reduction in depressive symptoms. These findings align with research in which stroboscopic stimulation has been shown to induce positive changes in the psychological state of patients. In addition, our collaborators (Winkler, Proeckl) have informally used stroboscopic light in clinics for over a decade, finding it to be more effective than conventional therapeutic approaches when treating depression (personal communication). These findings are also supported by suggestive animal research showing that stroboscopic light can significantly reduce depression-like behaviours.

We are also motivated by the resurgence of research into the potential therapeutic benefits of psychedelics, particularly for depression. It is broadly thought that the altered subjective experience induced by psychedelics, particularly the sense of awe, is key to their therapeutic effect. Since mental health symptoms primarily manifest in altered patterns of perception, emotion, and cognition, it is plausible that the most effective treatments will be those that

directly affect these aspects of human experience. From this perspective there are suggestive similarities between stroboscopically induced and psychedelic experiences: both involve vivid perceptual and emotional experiences, have been described as awe-inducing, and even transformative.

Preliminary data also suggest some similarities in the alterations in neural activity and thalamocortical interactions between strobe and psychedelic experiences, indexed by EEG and fMRI findings. However, while promising, psychedelic therapy lacks definitive evidence as a treatment for depression, as well as being controversial, and inaccessible for many. Our stroboscopic intervention potentially provides an accessible and readily controllable adjunct or alternative.

This broad evidence base and rationale motivates our overarching hypothesis that stroboscopic light stimulation will display a signal of therapeutic efficacy in alleviating symptoms associated with MDD.

This project focuses on mild to moderate forms of MDD which accounts for approximately 90% of depressive cases in the UK. There is therefore a vast group of MDD end users that could benefit, without the problematic side-effects or access barriers associated with conventional treatment options.

The current standard forms of treatment for depression can be divided into pharmacotherapy and psychotherapy. There are currently >30 antidepressants on the market, all of which are roughly equally effective. Approximately 56-60% of people with depression show some benefits from treatment with antidepressants. However, pharmacotherapy is often associated with problematic side effects, slow onset of therapeutic effects (4 to 6 weeks) and relapse. Pharmacotherapy is not generally considered to be an appropriate intervention for mild MDD due to these risks as well as the lack of clear separation vs. placebo for mild symptoms. Critically, although widely used in the treatment of depression, antidepressants show a non-responder rate of between 30-50% and in studies using representative samples of depressed patients only 11-30% of those who receive adequate pharmacotherapy achieve full remission.

Psychotherapy, such as cognitive behavioural therapy (CBT), is also a viable, though not fully effective treatment option for depression. A large meta-analysis of studies investigating the long-term effectiveness of CBT showed small to moderate effect sizes when compared to care-as-usual or a pill placebo. However, the timescales associated with psychotherapeutic treatment combined with challenging cost-effectiveness, local access barriers, and shortage of trained therapists make this approach difficult and costly to implement at scale. Attempts to circumvent some of these issues by using computerized cognitive-behavioural therapy (CCBT) has shown some potential but has been associated with high drop-out rates and little is known about the

acceptability of the therapy to patients. It is fair to say that the therapeutic effectiveness of CCBT within primary care remains unestablished.

Over the past decade, there has been a resurgence of research into the potential therapeutic benefits of psychedelic compounds, particularly for depression. Recent clinical research has found promising response rates when psychedelic-assisted psychotherapy is delivered to appropriately screened participants and in controlled settings. However, to date, there is limited definitive evidence for the effectiveness of psychedelic therapies, and they remain controversial and difficult to access due to legal restraints. Our non-pharmacological stroboscopic intervention delivers vivid altered perceptual and emotional experiences of the sort that may be key to psychedelic therapy, while remaining accessible, safe and scalable, potentially providing a much-needed complement or alternative.

Non-stroboscopic bright light therapy has become a standard treatment for both seasonal affective disorder (SAD) and non-seasonal forms of depression, through a theorised modulation of a person's natural circadian rhythm. However, most studies testing bright light therapy are small, with short durations and have methodological flaws. Therefore, the evidence for its efficacy, particularly for non-seasonal forms of depression, remains to be established.

The proposed intervention has multiple competitive advantages over conventional treatment options:

1. It is low risk. Patient risks associated with the intervention are minimal and the use of our rigorous safety screening protocol further mitigates risks. This protocol allowed nearly 40,000 people to safely take part in the Dreamachine stroboscopic experience. Based on recent prevalence rates of depressive symptoms within the UK population, it is possible that >6,000 of these individuals were experiencing depressive symptoms.
2. It displays a considerably reduced side-effect profile compared to traditional pharmacotherapeutic interventions.
3. It is well tolerated. Preliminary data from Dreamachine found that <2% of individuals who took part withdrew (subset of users n = 15,505), and in a subset from whom more detailed reports were obtained (n = 5,569), there were negligible uncomfortable side effects.
4. It displays a potential for high cost-effectiveness. The minimal setting, equipment and training associated with the intervention will likely reduce costs associated with delivery compared to traditional psychotherapeutic interventions.
5. It is accessible. The intervention has the potential to be flexibly deployed, allowing for rapid patient accessibility and benefits. It could be implemented in various settings such as in-clinic environments, group sessions, or even (with appropriate testing) in the person's own home.

6. It is efficient. In comparison to emerging psychedelic psychotherapeutic approaches, the intervention can be administered in brief sessions (e.e., 30 minutes) and its immediate experiential effects are tightly constrained to the treatment period. Psychedelic treatment sessions typically last for hours – again limiting accessibility.
7. The vivid visual and emotional experiences associated with a stroboscopic light session occur almost immediately. This suggests a potential for rapid onset of therapeutic effects for the intervention compared to both pharmaceutical and psychotherapeutic interventions.

Altogether, compared to existing and emerging treatment options, the proposed stroboscopic intervention is easy and efficient to administer, has a minimal side-effect profile, is scalable, and has the potential for cost-effectiveness, rapid onset of therapeutic effects, and for assimilation into existing treatment pathways.

Our primary market comprises clinics and front-line services that treat mild to moderate forms of MDD, which represents a sizable market. In Autumn 2022, around 1 in 6 adults (16% or 8,000,000 adults) reported depressive symptoms in Great Britain. If successful, the intervention could be tested within more severe forms of depression, including treatment-resistant forms, and other mental health conditions, such as post-traumatic stress disorder, anorexia nervosa, or adolescent depression and for use to enhance general health and well-being. Similarly, there is considerable potential for the intervention to be deployed flexibly in many different settings, to maximise patient accessibility and benefit.

B. EXPLANATION FOR CHOICE OF COMPARATORS

The aims of this study are to evaluate the safety and tolerability of exposure to stroboscopic light in MDD and collect critical data on the stroboscopic parameters that reliably elicit tolerable, comfortable, and engaging experiences, and the (control) parameters that cause minimal stroboscopic experiences.

Controllable parameters affecting the subjective intensity of stroboscopic experiences include luminance, stimulation frequency, rapid frequency alterations, and duty cycle. We will test each single parameter in separate stroboscopic sessions. Our aim is for the initial session to induce minimal effects, with subsequent sessions using a staircase method to gradually increase luminance, stimulation frequency, frequency transitions and duty-cycle change, corresponding to increased overall subjective intensity. While data from the Dreamachine shows a high tolerability to stroboscopic light in the general population (>40,000), it remains to be established if this is also true in people with MDD.

7. SPECIFIC OBJECTIVES OR HYPOTHESES

O1. Evaluate the safety and tolerability of exposure to stroboscopic light in MDD.

O2. Collect critical data on the stroboscopic parameters that reliably elicit tolerable, comfortable and engaging experiences and the (control) parameters that cause minimal stroboscopic experiences.

8. TRIAL DESIGN

This is a single-arm safety and tolerability study (with dose escalation).

METHODS: PARTICIPANTS, INTERVENTIONS, AND OUTCOMES

9. DESCRIPTION OF STUDY SETTING AND LIST OF COUNTRIES WHERE DATA WILL BE COLLECTED

Demographic information and inclusion criteria data will be collected online via Qualtrics; participants will be excluded at this point if they are not eligible based on the outlined inclusion and exclusion criteria.

Testing will take place within the Sussex Centre for Consciousness Science's laboratory, on the University of Sussex Falmer Campus. Participants are tested within a sound-proof booth with computer equipment to record their answers using the online-survey tool Qualtrics between strobe sessions, with the strobe light being placed on the outside of the window of the booth.

All testing will take place in Brighton, England.

10. INCLUSION AND ELIGIBILITY CRITERIA FOR PARTICIPANTS

Inclusion:

1. 18 years of age or older.
2. Willingness to take part in the study.
3. PHQ-9 score indicative of mild to severe depression (score of 5-27).

Exclusion:

1. Positive response to any question on the safety screening protocol (see attached).

2. Currently pregnant.

3. History of or current substance or drug abuse.

4. History of or current diagnosis of psychosis; bipolar disorder; Parkinson's Disease; dementia; Alzheimer's disease.

5. A history of traumatic brain injury (TBI).

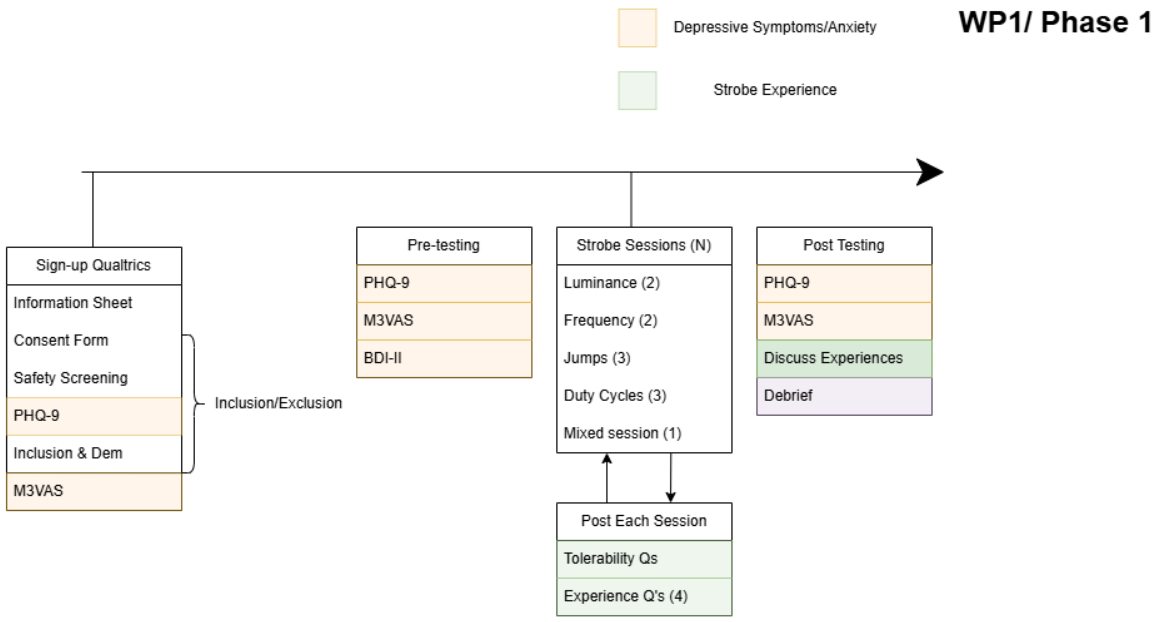
6. Presence of certain eye disorders such as retinal blindness, cataracts, retinal diseases of the eye and glaucoma.

A. INTERVENTIONS FOR EACH GROUP WITH SUFFICIENT DETAIL TO ALLOW REPLICATION, INCLUDING HOW AND WHEN THEY WILL BE ADMINISTERED

Within this tolerability study (WP1) we have opted for a single-arm design without a control group, as the primary objective is to assess the intervention's feasibility and tolerability rather than its efficacy. Feasibility studies are typically not designed to test efficacy but to determine whether an intervention can be successfully implemented. In this case, the primary objective is to evaluate tolerability rather than compare outcomes between conditions. In early-phase research, single-arm designs are common, especially when the aim is to gather initial safety and acceptability data before planning a controlled trial. Since this study focuses on participant-reported tolerability and adverse effects, a comparison group is not necessary for this initial evaluation.

Our primary measure of depressive symptomatology is the Patient Health Questionnaire-9 (PHQ-9), with secondary measures including the Maudsley 3-Item Visual Analogue Scale (M3VAS), and Beck’s Depression Inventory-II, all of which will be completed by participants before the study (see Figure 1).

Figure 1. Workflow for Work Package 1.



All stroboscopic stimulation will be delivered using a CE-certified commercial stroboscope, roXiva RX1, which consists of 16 LEDs with an overall maximum luminance of 16,000 lux at 0.5 meters. For comparison, light therapy lamps designed to treat Seasonal Affective Disorder (SAD) typically emit 10,000 lux, which is about 10% of the luminance from the sun on a clear day (Campbell et al., 2019); all luminance levels used in this study are well safety guidelines specified by the European Photobiological Safety Directive 2006/25/EC.

Within the current study, a maximum luminance of 3800 lux over the participant's (closed) eyes at a distance of 1 meter will be used. Previous research has administered stroboscopic light successfully to influence mood states; our research expands this literature by assessing the safety and tolerability of this approach in the MDD population (Johnson et al., 2024).

Participants will undergo 11 stroboscopic sessions of increasing subjective ‘intensity’, following a fixed order, each lasting 2 minutes. The first 10 sessions are divided into four 30-second sections to test incremental changes in parameters; luminance, stimulation frequency, rapid frequency changes, and duty cycles. Initial sections are designed to induce minimal effects, with subsequent sections using a staircase method to gradually increase the intensity of the stroboscopic experience (see Figure 2). The final session (session 11) will contain a combination of all tested parameters.

Figure 2. Individual Stroboscopic Stimulation Session Parameters for Work Package 1.

Session Number	Tested Parameters	Split	Steps
1	Luminance	4 x 30 sec	10, 30, 50, 70
2	Luminance	4 x 30 sec	70, 80, 90, 100
3	Frequency	4 x 30 sec	3, 5, 7, 9
4	Frequency	4 x 30 sec	9, 11, 13, 15
5	Frequency Shift Small	4 x 30 sec	3, 3.75, 4.69, 5.82 (multiplicative ratio of 1.25x base Hz, a major third)
6	Frequency Shift Moderate	4 x 30 sec	3, 4.5, 6.75,10.13 (multiplicative ratio of 1.5x base Hz, a perfect fifth)
7	Frequency Shift Larger	4 x 30 sec	3, 6.6, 14.52, 6.6 (multiplicative ratio of 2.2x base Hz, close to a ninth)
8	Duty Cycle Shift Small	4 x 30 sec	50, 55, 60, 65
9	Duty Cycle Shift Moderate	4 x 30 sec	40, 50, 60, 70
10	Duty Cycle Shift Larger	4 x 30 sec	25, 50, 75, 50
11	Dynamic sequence	120 sec	Combination of the above parameters

After each 2-minute session, participants will be asked whether they had any side effects; if they select no, they will not be asked any further information regarding the tolerability of the current session. If participants indicate that they experienced adverse effects, they will be presented with a list of symptoms from the Visual Discomfort Questionnaire to select the frequency at which each symptom occurred (Vinkers et al., 2024). Any reported side effect will then be rated on a 10-point scale, this will be referred to as the *tolerability score* or symptom discomfort score, the scale ranges from 0 (no symptom discomfort) to 10 (worst possible symptom discomfort), with 3 indicating mild symptom discomfort, 5 moderate symptom discomfort, and >7 severe symptom discomfort. Any report of a scorer >7 will result in that parameter's testing being stopped immediately to avoid further discomfort.

Participants will also report their overall experience on a 0-100 sliding scale via Qualtrics, asking the participant to report how engaging, pleasurable, overall uncomfortable, and sleepy each session was.

After each round of questions, participants will have an opportunity to share their thoughts on the session and also have a break.

To ensure that the experimental procedure has not inadvertently increased participants' depressive symptoms, participants will fill out the M3VAS change and the PHQ-9 again at the end of the testing session. If participants report a deterioration in well-being as indexed by any increase in M3VAS scores in the pre-to-post measurements, support will be offered and the participant referred to relevant sources of support, such as the University of Sussex-specific counselling services for students, as well as their GP, general non-emergency mental health support, or local A&E services, depending on the severity of symptoms.

After the administration of all sessions and questionnaires, participants will be debriefed; this will be the end of the testing session.

B. CRITERIA FOR DISCONTINUING OR MODIFYING ALLOCATED INTERVENTIONS FOR A GIVEN TRIAL PARTICIPANT

As this study is collecting preliminary data to inform the development of a stroboscopic intervention in WP2, we will not be discontinuing the intervention unless requested to by the participant;however, in the case of the current experiment if participants report a tolerability score of 7 or above, thatarm of the study will be halted immediately. If an adverse medical reaction occurs, all testing with that participant will be halted.

C. STRATEGIES TO IMPROVE ADHERENCE TO INTERVENTION PROTOCOLS, AND ANY PROCEDURES FOR MONITORING ADHERENCE

As this is a one-time (1hr) experiment, the adherence will only be monitored within the protocol of the study. Online pre-screening and consent collection ensure informed participation. Researchers will monitor participant experiences throughout testing and offer flexibility in scheduling when needed. Participants receive 10 GBP per hour or SONA credits for engagement with this study.

Experiments are run in the laboratory with a researcher present at all times; participants will be guided and monitored through the entirety of the experiment, guaranteeing the correct administration of the study protocol. All researchers follow an agreed-upon script to reduce researcher bias across the study.

D. RELEVANT CONCOMITANT CARE AND INTERVENTIONS THAT ARE PERMITTED OR PROHIBITED DURING THE TRIAL

Participants undergoing psychotropic treatment or additional talk-based therapeutic interventions are not excluded from participation in this study, but the medication or supplement and self-reported familiarity with their psychotropic treatment will be recorded.

12. PRIMARY, SECONDARY, AND OTHER OUTCOMES, INCLUDING THE SPECIFIC MEASUREMENT VARIABLE, ANALYSIS METRIC, METHOD OF AGGREGATION, AND TIME POINT FOR EACH OUTCOME; EXPLANATION OF THE CLINICAL RELEVANCE OF CHOSEN EFFICACY AND HARM OUTCOMES IS STRONGLY RECOMMENDED

Primary outcome:

- Safety outcomes: no adverse medical incidents (no medical intervention needed)
- Maximum tolerability score per 30 second section (0-10 scale)

  Data from Dreamachine suggests a high safety and tolerability profile to stroboscopic stimulation in the general population. However, we need to assess if this is also th case in MDD

  The safety outcomes are crucial in assessing the risks of stroboscopic light for people with MDD. If medical intervention is required due to the administration of (certain parameters) of strobe light, their administration will not be appropriate in this population.

  The tolerability score will be used to determine which parameters are appropriate for developing the WP2 intervention. Tolerability scores above 7 indicate severe discomfort due to associated side effects. Strobe light parameters that elicit a tolerability score exceeding 7 with an 80% confidence limit will be considered inappropriate for administration to the MDD population and will not be included in the intervention.

Secondary outcomes:

Secondary outcomes will only be explored through exploratory analyses between sessions and participants, and will include the following measures:

- Type, frequency and intensity of symptoms
- Feasibility, participant recruitment numbers over time
- Participants' report of arousal, enjoyment, overall discomfort and engagement as reported through single items (scale 0-100).

The type, frequency, and intensity of side effects associated with strobe light parameters will provide early insights into potential mild symptoms that strobe light may cause in individuals with MDD, serving as an early indicator for future treatments.

Feasibility does not have direct clinical implications beyond being an estimate of the local population with MDD and general interest in experiencing strobe.

Participants' arousal, enjoyment, overall discomfort and engagement do not have direct clinical implications, but will be analysed to understand trends of participants' experiences during different strobe light parameters and used to inform the development of the intervention in WP2.

12.1. RATIONALE FOR THE SELECTION OF THE DOMAIN FOR THE TRIAL'S PRIMARY OUTCOME

This study aims to evaluate the safety and tolerability of exposure to stroboscopic light in individuals with MDD and to collect critical data on the stroboscopic parameters that reliably elicit tolerable, comfortable, and engaging experiences.

Tolerability is assessed by participants selecting which side effects they experienced, if any. The potential side effects are drawn from three of the Visual Discomfort Questionnaire's (VDQ) subscales: sickness, eye discomfort and head discomfort (Vinkers et al., 2024). The VDQ was developed to measure the discomfort caused by various visual stimuli. In this study, the subscale for side effects on vision is omitted, as participants will have their eyes closed during the strobe sessions, and visual hallucinations are considered part of the experience. A 10-point scale is used to signify the severity of symptom discomfort, allowing for an immediate understanding of participants' tolerance levels; this measure comprises their tolerability score.

12.2. IF THE ANALYSIS METRIC FOR THE PRIMARY OUTCOME REPRESENTS WITHIN-PARTICIPANT CHANGE, DEFINE AND JUSTIFY THE MINIMAL IMPORTANT CHANGE IN INDIVIDUALS

This does not apply to the current study.

12.3. IF THE OUTCOME DATA COLLECTED ARE CONTINUOUS BUT WILL BE ANALYZED AS CATEGORICAL, SPECIFY THE CUTOFF VALUES TO BE USED

This is not applicable to this research study.

12.4. IF OUTCOME ASSESSMENTS WILL BE PERFORMED AT SEVERAL TIME POINTS AFTER RANDOMIZATION, STATE THE TIME POINTS THAT WILL BE USED FOR ANALYSIS

No randomisation or blinding will take place in this study.

After each 2-minute strobe session participants will answer questions regarding potential side effects, tolerability and their overall stroboscopic experience.

12.5. IF A COMPOSITE OUTCOME IS USED, DEFINE ALL INDIVIDUAL COMPONENTS OF THE COMPOSITE OUTCOME

In addition to the session-specific tolerability rating, we will ask participants to indicate (if possible) in which 30-second section of a session these side effects occurred. The session-specific tolerability score is defined as the highest tolerability score reported for any present side effects during that block.

13.

TIME SCHEDULE OF ENROLLMENT, INTERVENTIONS, ASSESSMENTS, AND VISITS FOR PARTICIPANTS (A SCHEMATIC DIAGRAM IS HIGHLY RECOMMENDED)

Pre-trial: Through an online Qualtrics survey: information sheet provided to the participant, consent form, pre-screening and demographic questions, PHQ-9 and M3VAS .

Weeks 1-6: Experimentation, 60 minutes per participant.

Weeks 6+: Data analysis and research and development to create the intervention that will be used in WP2.

14. ESTIMATED NUMBER OF PARTICIPANTS NEEDED TO ACHIEVE STUDY OBJECTIVES AND HOW IT WAS DETERMINED

Based on guidelines for the required sample size for a pilot/feasibility trial to precisely estimate the standard deviation (SD) of a normally distributed variable (session tolerability score) we will use a sample size of 25 (Whitehead et al., 2016). Anticipating a maximum dropout rate of 20% the total sample size required for this study is 32 (WP1).

14.1. DEFINE AND JUSTIFY THE TARGET DIFFERENCE BETWEEN TREATMENT GROUPS

Within this research, no treatment groups are differentiated.

15. STRATEGIES FOR ACHIEVING ADEQUATE PARTICIPANT ENROLLMENT TO REACH TARGET SAMPLE SIZE

Participants will be recruited through several routes:

1. University of Sussex (UoS) internal recruitment system, SONA
2. Advertisements in public and community spaces on the University of Sussex Falmer Campus (posters, recommendations or email lists)

To compensate participants for their time and effort, they will receive 10 GBP per hour or 4 SONA credits per hour.

METHODS: ASSIGNMENT OF INTERVENTIONS

16.

A. METHOD OF GENERATING THE ALLOCATION SEQUENCE AND LIST OF ANY FACTORS FOR STRATIFICATION

This is not applicable to this research study.

B. MECHANISM OF IMPLEMENTING THE ALLOCATION SEQUENCE, DESCRIBING ANY STEPS TO CONCEAL THE SEQUENCE UNTIL INTERVENTIONS ARE ASSIGNED

This is not applicable to this research study.

C. WHO WILL GENERATE THE ALLOCATION SEQUENCE, WHO WILL ENROLL PARTICIPANTS, AND WHO WILL ASSIGN PARTICIPANTS TO INTERVENTIONS

This is not applicable to this research study.

17.

A. WHO WILL BE BLINDED AFTER ASSIGNMENT TO INTERVENTIONS, AND HOW

This is not applicable to this research study.

B. IF BLINDED, CIRCUMSTANCES UNDER WHICH UNBLINDING IS PERMISSIBLE, AND PROCEDURE FOR REVEALING A PARTICIPANT'S ALLOCATED INTERVENTION DURING THE TRIAL

This is not applicable to this research study.

18.

A. PLANS FOR ASSESSMENT AND COLLECTION OF OUTCOME, BASELINE, AND OTHER TRIAL DATA, INCLUDING ANY RELATED

PROCESSES TO PROMOTE DATA QUALITY AND A DESCRIPTION OF STUDY INSTRUMENTS ALONG WITH THEIR RELIABILITY AND VALIDITY

A1. DESCRIBE WHAT IS KNOWN ABOUT THE RESPONSIVENESS OF THE STUDY INSTRUMENTS IN A POPULATION SIMILAR TO THE STUDY SAMPLE

Patient Health Questionnaire-9 (PHQ-9):

This scale was developed to diagnose MDD and is now a widely used measure within health care services. The scale was developed to be in line with the DSM-V factors for depression and has been shown to correlate with other measures for MDD and quality of life measures (Kroenke et al., 2016). Its reliability has been shown to be good, with 5-point shifts signifying a clinically relevant change in symptoms (Lowe et al., 2004). Within the UK's National Health Service (NHS), the PHQ-9 is routinely employed as the standard measure for depression across all patients. Its brevity and ease of use make it suitable for both initial screening and ongoing monitoring of participants.

The Maudsley 3-Item Visual Analogue Scale (M3VAS):

The M3VAS is a concise tool designed to assess core symptoms of Major Depressive Disorder (MDD), specifically low mood and anhedonia. Comprised of three items, the M3VAS utilizes a visual analogue format to capture the severity of these symptoms. Initial validation studies demonstrated that total M3VAS scores correlate strongly with the 16-item Quick Inventory of Depressive Symptomatology-Self-Report (QIDS-SR-16), indicating good convergent validity (Moulton et al, 2021).

Beck Depression Inventory - 2 (BDI-II):

The BDI-II is a 21-item self-report instrument designed to assess the severity of depressive symptoms over the past two weeks, aligning with DSM-IV criteria. It has demonstrated high test-retest stability, internal consistency, clinical sensitivity, and construct validity (Whisman et al., 2000; Wang & Gorenstein, 2013). Given its robust psychometric properties and widespread use, the BDI-II is an appropriate supplementary measure for assessing depression in both clinical and research settings.

A2. DESCRIBE WHO WILL ASSESS THE OUTCOME

Outcomes will be assessed within the research team, with statistical oversight by the project's medical statistician, Prof. Bremner, alongside additional statistical support by Barnett.

B. PLANS TO PROMOTE PARTICIPANT RETENTION AND COMPLETE FOLLOW-UP, INCLUDING ANY LIST OF ANY OUTCOME DATA TO BE COLLECTED FOR PARTICIPANTS WHO DISCONTINUE OR DEVIATE FROM INTERVENTION PROTOCOLS

This research study consists of a single experimental session. Between sign-up and testing in the laboratory, clear email communication will be kept with participants to ensure they understand the study instructions (1 email post sign-up and a reminder email the day before testing takes place). After testing, participants will be invited to submit their email addresses to be contacted for related future research studies.

19. PLANS FOR DATA ENTRY, CODING, SECURITY, AND STORAGE, INCLUDING ANY RELATED PROCESSES TO PROMOTE DATA QUALITY

Data will be stored and encryptedd in University of Sussex (UoS) approved secure databases. Identifying information, such as name and email, will be deleted 2 weeks post-study completion as specified in the consent form. Anonymised data will be stored indefinitely.

Periodic data checks through Qualtrics will be carried out, with data backups being performed regularly to mitigate the risk of data corruption.

20.

A. STATISTICAL METHODS FOR ANALYZING PRIMARY AND SECONDARY OUTCOMES

To test whether 30-second sections within the strobe sessions are tolerable, participants' maximum tolerability score within each section is considered. If participants don't report any negative symptoms, their tolerability score across the relevant sections will be recorded as 0.

A parameter's 30-second section will be considered tolerable if, across participants, the upper limit of the 80% confidence interval for reported tolerability scores is less than 7.

Secondary outcomes will be evaluated through exploratory analyses, such as examining the frequency of any side effects, engagement, arousal, overall discomfort and enjoyment. These analyses will be descriptive, utilizing data visualizations and descriptive statistics to explore patterns across sessions, both within and between participants.

A1. DESCRIBE ANY PLANNED METHODS TO ACCOUNT FOR MULTIPLICITY IN THE ANALYSIS OR INTERPRETATION OF THE PRIMARY AND SECONDARY OUTCOMES

This is not applicable to this research study.

B. METHODS FOR ANY ADDITIONAL ANALYSES

Secondary outcomes will be explored through data descriptors (i.e. means, standard deviations) and graphs comparing them between sessions within and between participants. Due to expected low power of any such comparisons no inferential statistical analysis will be performed. These explorations will be used to identify potential trends and patterns, but will not be used to infer any relationships between variables.

C. DEFINITION OF ANALYSIS POPULATION RELATING TO PROTOCOL NON-ADHERENCE, AND ANY STATISTICAL METHODS TO HANDLE MISSING DATA

Data from participants who do not attend the experimental testing or withdraw before the administration of any strobe sessions will not be included in the analyses of the intervention's tolerability.

However, if a participant discontinues their participation due to discomfort during the strobe sessions, their partial data up to the point of withdrawal will be included in the analysis.

Data from all participants completing the sign-up form, regardless of their eligibility will be recorded and stored to quantify interest in these strobe light experiments.

The data of any participant requesting their data to be withdrawn from the study, within 2 weeks of the end of testing will be deleted and excluded from all analysis.

METHODS: MONITORING

21.

A. COMPOSITION OF DATA MONITORING COMMITTEE; SUMMARY OF ITS ROLE AND REPORTING STRUCTURE; STATEMENT OF WHETHER IT IS INDEPENDENT FROM THE SPONSOR AND COMPETING INTERESTS; AND REFERENCE TO WHERE FURTHER DETAILS ABOUT ITS CHARTER CAN BE FOUND (OR AN EXPLANATION OF WHY A DMC IS NOT NEEDED)

In our study, data management will be overseen by the Project Management Committee (PMC), comprising Schwartzman, Seth, Stone, and Bremner. An external Data Monitoring Committee (DMC) is not necessary for this study.

B. DESCRIPTION OF ANY INTERIM ANALYSES AND STOPPING GUIDELINES, INCLUDING WHO WILL HAVE ACCESS TO THESE INTERIM RESULTS AND MAKE THE FINAL DECISION TO TERMINATE THE TRIAL

Based on guidance from the project'statistician, recruitment will cease once a sample size of 32 participants is achieved. Any participants already scheduled for testing at that point will complete their sessions, and their data will be included in the analysis.This monitoring will be done by the PMC, PI, research assistant and associated PhD student.

22. PLANS FOR COLLECTING, ASSESSING, REPORTING, AND MANAGING SOLICITED AND SPONTANEOUSLY REPORTED ADVERSE EVENTS AND OTHER UNINTENDED EFFECTS OF TRIAL INTERVENTIONS OR TRIAL CONDUCT

In our study, we have established comprehensive procedures for collecting, assessing, reporting, and managing both solicited and spontaneously reported adverse events (AEs) and other unintended effects related to trial interventions or conduct. After each 2-minute strobe session, participants will be prompted to report any discomfort or side effects experienced during the session. They will rate any symptom related discomfort on a scale from 0 to 10. If a participant reports severe symptom discomfort (score >7), testing sessions involving increases of that specific parameter will be halted for that participant to prevent further discomfort, and partial data collected up to that point will be retained for analysis. Any severe adverse clinically relevant events or significant concerns will be promptly reported to the Co-Investigator, Prof. James Stone. Stone has extensive experience as PI on multiple clinical trials and experimental medicine studies in patients; he has worked as a psychiatrist for 25 years, including 16 years as a consultant (with expertise in affective disorders, psychosis, and liaison psychiatry). Participants will complete the M3VAS and PHQ-9 assessments at the start and end of the experiment to monitor their well-being. If a participant's well-being deteriorates, they will be referred to appropriate mental health services, and Prof. James Stone will be informed. In rare cases of psychological distress or any concerns from the researchers, Prof. James Stone will be notified to determine appropriate actions. These procedures are designed to ensure participant safety and comply with regulatory requirements for adverse event reporting in clinical trials.

23. FREQUENCY AND PROCEDURES FOR AUDITING TRIAL CONDUCT, IF ANY, AND WHETHER THE PROCESS WILL BE INDEPENDENT FROM INVESTIGATORS AND THE SPONSOR

All researchers will follow a script and calibrate their conduct periodically through internal reviews.

ETHICS AND DISSEMINATION

24. PLANS FOR SEEKING RESEARCH ETHICS COMMITTEE/INSTITUTIONAL REVIEW BOARD APPROVAL

Ethical approval has been obtained by the local ethical research committee at the University of Sussex, ethical review number: ER/LK344/4.

25. PLANS FOR COMMUNICATING IMPORTANT PROTOCOL MODIFICATIONS TO RELEVANT PARTIES

Any changes to the protocol and any other aspects of the research will be communicated with all parties in the research team.

26.

A. WHO WILL OBTAIN INFORMED CONSENT OR ASSENT FROM POTENTIAL TRIAL PARTICIPANTS OR AUTHORIZED SURROGATES, AND HOW

Before participants begin the online pre-screening, they will be provided with full information about the study and provide online consent to take part in the study.

The consent form will make clear that participants can withdraw from the experiment at any time without penalty.

Should a participant want to withdraw at any point, all that will be required is an email or verbal communication requesting their withdrawal to the PI Dr. David Schwartzman or to any other researcher in the project (contacts provided on the information sheet and consent form).

B. ADDITIONAL CONSENT PROVISIONS FOR COLLECTION AND USE OF PARTICIPANT DATA AND BIOLOGICAL SPECIMENS IN ANCILLARY STUDIES, IF APPLICABLE

Participants are informed and consent to their fully anonymised data being stored indefinitely and used in future studies.

27. HOW PERSONAL INFORMATION ABOUT POTENTIAL AND ENROLLED PARTICIPANTS WILL BE COLLECTED, SHARED, AND MAINTAINED IN ORDER TO PROTECT CONFIDENTIALITY BEFORE, DURING, AND AFTER THE TRIAL

All information collected during this research will be kept strictly confidential and in compliance with GDPR guidelines provided by the University of Sussex. Initially, participant data will be linked to their name and email address to facilitate withdrawal requests, should they wish to have

their data removed. This link will remain in place until 2 weeks after the experiment is completed (cut-off dates will be provided in the information sheet and consent form). After this time all data will be anonymized meaning that their details cannot be matched back to them, and they therefore cannot withdraw their data after this time. This point is clearly described on the consent form.

To further protect confidentiality, no information will be retained that can be connected to specific individuals beyond 2 weeks after testing. No personally identifiable data will be kept in the recorded data and this unidentifiable data will be stored in an approved data management system (i.e., Box or OneDrive). To maintain complete confidentiality, data from the consent form will be stored separately to all other data within this study. After 5 years, the consent form data will be deleted.

Anonymised research data will be retained indefinitely, as stated in the consent form. This long-term retention ensures that the dataset remains available for future research purposes and allows for verification of the findings from this study if necessary. Only the PI, Dr. David Schwartzman, along with project researchers Danny Nacker and Luise Kalus, will have access to the personal information collected in this study. At no point will personal information be shared with third parties, and all research data will be used solely for academic purposes. These measures ensure that participant confidentiality is rigorously maintained before, during, and after the trial.

28. FINANCIAL AND OTHER COMPETING INTERESTS FOR PRINCIPAL INVESTIGATORS FOR THE OVERALL TRIAL AND EACH STUDY SITE

DJS and AKS, are collaborators on Collective Act's Dreamachine programme. DJS received funding from the UK Govt via Collective Act to support this collaboration. This funding was independent of the current study. The company roXiva provided a commercial stroboscope, RX1, for use in this study at no cost.

29. STATEMENT OF WHO WILL HAVE ACCESS TO THE FINAL TRIAL DATASET, AND DISCLOSURE OF CONTRACTUAL AGREEMENTS THAT LIMIT SUCH ACCESS FOR INVESTIGATORS

No blinding takes place in this case. The testing researchers (PI, research assistant and PhD student) have access to the data on Qualtrics for monitoring. After testing is complete data will be provided to the statistician of the team (Prof Stephen Bremner) for statistical testing.

30. PROVISIONS, IF ANY, FOR ANCILLARY AND POST-TRIAL CARE, AND FOR COMPENSATION TO THOSE WHO SUFFER HARM FROM TRIAL PARTICIPATION

Prof. James Stone has agreed to provide support for both the researchers and participants in this study. If at any point in the study the researchers become concerned about the mental health of a participant, James has provided the research team with guidance on the clinically appropriate methods for directing the participant to the appropriate mental health support services. Prof. James Stone has also agreed, if necessary, to be available to come into the lab to facilitate giving the appropriate assistance directly to the participant.

At the start and the end of the experiment participants will fill out the M3VAS; if participants' well-being deteriorates, they will be referred to mental health services and Prof James Stone will be informed.

In rare cases of psychological distress, or any concerns arise from the researchers, Prof. James Stone will be informed.

31.

A. PLANS FOR INVESTIGATORS AND SPONSOR TO COMMUNICATE TRIAL RESULTS TO PARTICIPANTS, HEALTHCARE PARTICIPANTS, THE PUBLIC, AND OTHER RELEVANT GROUPS, INCLUDING ANY PUBLICATION RESTRICTIONS

Peer-reviewed journals (ideally open-access) and public dissemination via UoS/SCCS.

B. AUTHORSHIP ELIGIBILITY GUIDELINES AND ANY INTENDED USE OF PROFESSIONAL WRITERS

We will follow the ICMJE authorship criteria, for assigning authorship to any resulting publications from this project.

C. PLANS, IF ANY, FOR GRANTING PUBLIC ACCESS TO THE FULL PROTOCOL, PARTICIPANT-LEVEL DATASET, AND STATISTICAL CODE

Anonymised research data will be retained indefinitely; this is mentioned clearly in the consent form. This will allow data to be available for future research purposes and so that the results of this research project are open to investigation if needed. The results obtained from the research will be published in open-access publications, ensuring widespread availability and dissemination of the findings.

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APPENDICES

32. MODEL CONSENT FORM AND OTHER RELATED DOCUMENTATION GIVEN TO PARTICIPANTS AND AUTHORIZED SURROGATES

32a. Information Sheet

Exploring the Safety and Tolerability of Strobe Light in People with Depression

Principal Investigator: Dr. David Schwartzman (d.schwartzman@sussex.ac.uk)
Danny Nacker (d.nacker@sussex.ac.uk)
Luise Kalus (lk344@sussex.ac.uk)

Introduction

I would like to take this opportunity to thank you for your interest in taking part in our study. Before you decide whether you would like to participate you need to understand why the research is being done and what it would involve. Please take time to read the following information carefully and do not hesitate to ask if there is anything that is not clear or if you would like more information.

What is the purpose of the study?

Stroboscopic light, bright and quickly flashing lights, have been used to induce stroboscopic experiences, which may for example include visual experiences.
This study aims to test whether individuals with mild to moderate depression can safely and comfortably take part in strobe light experiences. We will also test what parameters lead to a comfortable and engaging experience in people with depression, and which ones lead to minimal stroboscopic experiences.

Who can take part in this study?

We invite people with symptoms in line with mild and moderate depression to take part in this study, **you do not require a formal diagnosis to take part**. You must be 18 or older to take part in this study.
You will complete questionnaires to determine your eligibility and a safety screening form to ensure your safety during the stroboscopic experience before taking part in the study.
Please note that:
Meeting the criteria to participate in this study is not a clinical diagnosis of any condition.

Do I have to take part in this study?

No, participation is entirely voluntary. After you have read this information sheet and before participating you will be asked to sign a consent form to show you agree to take part. Should you agree to participate you will nonetheless be free to withdraw at any time, without giving a reason, and will still be paid for your time or receive the SONA points.

What will I do if I take part in this study?

After reading this information sheet and providing your consent, you will be asked to fill out a standardised questionnaire about any depressive symptoms you may have. Along with some questions regarding any current or past treatment for depression. Following this you will complete a safety screening survey regarding strobe light exposure and any pre-existing risk factors you may have. Please do not take part in this study if you believe that answering any questions on these topics will negatively impact your wellbeing.
If you qualify for this study, you will be asked to attend a single 1-hour testing session at the Sussex Centre for Consciousness Science. During this testing session you will sit with your eyes closed in front of a strobe light that flickers at different frequencies and brightnesses. You will be sent copies of all relevant information by email before taking part. The sessions are conducted individually by one of our trained researchers, ensuring your safety and comfort. The brightness of the light will never exceed what you may experience on a bright sunny day. Strobe light at differing frequencies has been shown to induce interesting conscious content, such as geometric visual experiences and a loss of connection to your body.
You will be asked to repeatedly report your experience of the strobe at different frequencies and brightnesses through short questionnaires throughout this testing session If, at any point during the session, you report or communicate discomfort to the researcher, the strobe light exposure will be immediately stopped.

After this testing session you will receive payment/SONA points and will be asked whether we may contact you for further testing in the future.

What are the possible benefits of taking part?

To compensate you for your time and effort, you will receive either 4 SONA credits per hours or £10 per hour.
Additionally, the knowledge gained from this study may inform future treatment options for depression as well as being of general theoretical interest. Although there is no direct benefit for you, in participating in the study you will know that you have made a valuable contribution to these objectives.

Are there any risks involved in taking part?

The topics involved in this study may be more sensitive to some than others. A small number of questions about psychological symptoms involve asking about low mood and suicidal thoughts. **If you feel that answering any of these questions will impact negatively on your wellbeing or cause significant lasting distress, then it is important for your wellbeing not to take part.** If you are concerned about your own emotional wellbeing or mental health, then here are some sources of support to consider:
Student Life Centre (University of Sussex)
Website: https://www.sussex.ac.uk/studentlifecentre/
Phone: 01273 876767
Email: studentlifecentre@sussex.ac.uk
https://www.mind.org.uk/information-support/types-of-mental-health-problems/seasonal-affective-disorder-sad/about-sad/
https://www.supportline.org.uk/problems/depression/
Although we have all been exposed to strobe lights at some point in our lives, flashing lights may in extremely rare cases induce seizures in susceptible individuals, or may cause anxiety and discomfort and in some people migraines. It is important that if you have a sensitivity to strobe lights or frequent migraines that you do not take part in this experiment, and that you have answered the questionnaires sent to you before you take part in this experiment to reduce these risk factors (e.g., history of epilepsy, high anxiety...).

Who has approved this study?

The project reference number is ER/LK344/4. If you have any ethical concerns, please contact the ethics chair (crecscitec@sussex.ac.uk). University of Sussex has insurance in place to cover its legal liabilities in respect of this study.

What if I later have a concern about this study?

If you have any concerns while taking part in this study, you can contact the principal investigator Dr David Schwartzman (d.schwartzman@sussex.ac.uk), the clinical lead Prof James Stone (j.stone@bsms.ac.uk), or researchers Danny Nacker (d.nacker@sussex.ac.uk) and Luise Kalus (lk344@sussex.ac.uk).

What will happen to my data and will it be kept confidential?

All information collected about you during the course of the research will be kept strictly confidential, your data will be linked to your name until 2 weeks after the experiment is completed (ESTIMATED TESTING END DATE), allowing you to withdraw your data during this period if you wish. After this time your data will be anonymised meaning that your details cannot be matched back to you and your data cannot be removed.

If you choose to provide your email address to be contacted for future studies, this email will not be connected to any information or data you provide as part of this study.

What will happen to the results of this study?

The results from studies such as this are normally presented internally and may be submitted for publication in a scientific journal. Any of your data from this study that is presented in any form will be totally anonymous.

Thank you for your interest in this study
Dr. David Schwartzman
Postdoctoral Research Fellow. The Sussex Centre for Consciousness Science

32b. Consent Form

Consent Form

Exploring the Safety and Tolerability of Strobe Light in People with Depression

Please tick each of the following statement to show that you have understood them and consent to them as part of this study:

Voluntary Nature of the Study/Confidentiality: Participation in this study is entirely voluntary and you may refuse to continue at any point or ask the researchers any questions. Your name will temporarily be connected to your data, this link will be erased 2 weeks after the completion of this study and a participant number will then be used for further identification purposes. Your personal data will not be released to anyone outside the project.

- I agree to take part in the University of Sussex research project described in the information page. I have read and understood the Explanatory Statement, which will be sent to me by email for my records. I also understand that I am free to withdraw my data by the EXPECTED CUT-OFF DATE, 2 weeks after the experiment, is completed by emailing one of the researchers (Dr. David Schwarzman: d.schwartzman@sussex.ac.uk, Danny Nacker: d.nacker@sussex.ac.uk, or Luise Kalus: lk344@sussex.ac.uk).
- I understand that any information I provide is confidential, and that no information that I disclose will lead to the identification of any individual in the reports on the project, either by the researcher or by any other party.
- I understand that my participation is voluntary, that I can choose not to participate in part or all of the project, and that I can withdraw at any stage of the project without being penalised or disadvantaged in any way.

- I understand that my personal data will be used for the purposes of this research study and will be handled in accordance with Data Protection legislation. I understand that the University's Privacy Notice provides further information on how the University uses personal data in its research.
- I understand that my data will be stored with my name EXPECTED CUT-OFF DATE, afterwards my data will be stored in a de-identified way (e.g. using ID numbers not names). If I indicate that I want to be contacted for a future study at the end of this study, my email address will be stored separately from all other data collected. Electronic data will be stored securely on a university managed system, and hard-copies will be stored behind a locked door.
- I understand that my anonymised research data will be retained indefinitely.
- I understand that such information will be treated as strictly confidential and handled in accordance with the Data Protection Act 2018.
- This study has been approved by the Sciences and Technology Cross-Schools Research Ethics Committee. The project reference number is ER/LK344/4. If you have any ethical concerns, please contact the ethics chair (crecscitec@sussex.ac.uk). University of Sussex has insurance in place to cover its legal liabilities in respect of this study.
- By ticking this box, I confirm I have no history of seizures or migraines.

I DO CONSENT

I DO NOT CONSENT

Please provide your first and last name:
Please provide you email address (it will only be used to provide you with relevant information regarding this research project, including sending you a copy of the information sheet and this consent form):

32c. Debrief

Exploring the Safety and Tolerability of Strobe Light in People with Depression

Debriefing Document

In humans, stroboscopic light on closed eyes, at certain frequencies, typically gives rise to vivid visual experiences (e.g., colours, geometric patterns, movement, complex scenes), as well as, for some people, powerful emotional responses. Recently, we completed a large-scale public art-science experience, the Dream Machine, which enabled more than 30,000 people to safely experience visual hallucinations induced by strobe light. Everyone participating in this event had a unique experience, despite being exposed to the same flickering white light.
The goal of the current study is to test the tolerability and safety of strobe light in people with depression and which strobe parameters lead to engaging experiences. You were invited to a testing session during which you rated your comfort and side effects when exposed to strobe light at different luminance, frequency and rapid frequency, this will help us understand what types of strobe light are safe for people with depression. Your rating of your visual and conscious experiences during each strobe sessions will help us develop engaging strobe sequences for people with depression.
If you are concerned about your own emotional wellbeing or mental health, then here are some sources of support to consider:

https://www.mind.org.uk/information-support/types-of-mental-health-problems/seasonal-affectivedisorder-sad/about-sad/

If you are a student at the University of Sussex:
Student Life Centre (University of Sussex)
Website: https://www.sussex.ac.uk/studentlifecentre/
Phone: 01273 876767 Email: studentlifecentre@sussex.ac.uk

If you have any question or concerns about this study, please get in touch with the lead researcher Dr David Schwartzman (d.schwartzman@sussex.ac.uk), Danny Nacker (d.nacker@sussex.ac.uk), or Luise Kalus (lk344@sussex.ac.uk).

Thank you for your participation in this study.
Dr. David Schwartzman - Postdoctoral Research Fellow.
The Sussex Centre for Consciousness Science

32d. Safety Screening Protocol

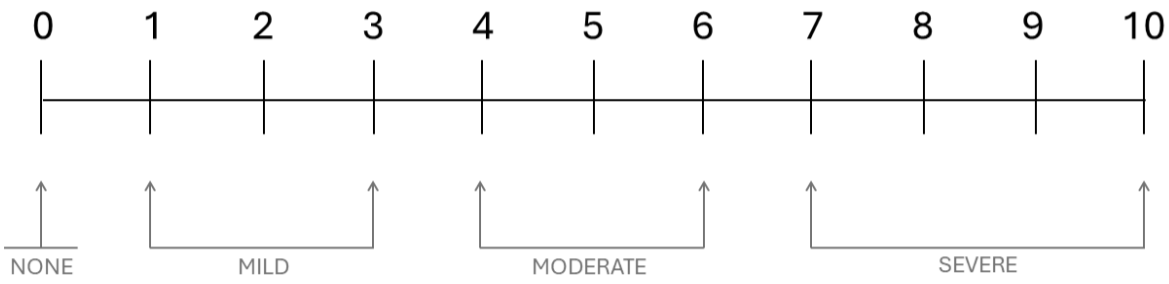
Do any of the following apply to you? Please answer Yes or No for each question.

Have you ever been told that you have or had epilepsy?	Yes/No
Have you ever had a seizure?	Yes/No
Has anyone in your immediate family, including your parents, siblings or second-degree relatives, been told that they have epilepsy or suffer from seizures?	Yes/No
Do you find sunlight, bright or flickering lights uncomfortable?	Yes/No
Have you ever had an adverse reaction to flickering or bright lighting?	Yes/No
Do you suffer from frequent or severe headaches including migraines?	Yes/No
Are you currently pregnant?	Yes/No

33e. Tolerability Questions

Participants be shown the list of symptoms they reported to have experienced and will rate them as follows:

How much discomfort did the symptoms to have experienced caused you, select a number from the discomfort scale.



32f. Demographic Questions

How old are you?	Number Input
What is your biological sex?	Female
	Male
	Other
What is your gender? (if you feel comfortable to share this)	Female
	Male
	Other
I am currently experiencing symptoms associated with depression, such as low mood or sadness, for extended periods of time.	Yes
	No
Do your symptoms of depression display a seasonal pattern? Are your symptoms usually more apparent and more severe during the winter?	Yes
	No

If you answered 'Yes' please provide more detail about your seasonal pattern of depression.	Text Input
Are you currently taking any medications, herbs, or supplements to treat your depression?	Yes
	No
If you answered 'Yes', this is not necessarily a problem for you to take part in this study. Please provide details of the treatment, including the name, dosage, and frequency of use.	Text Input
Have you been taking this medication long enough to consider it as familiar to you?	Yes
	No
	I don't know
Are you planning to **change** or **start treatment** for your depressive symptoms in the next EXPECTED TESTING DURATION, this includes therapy, medication or other interventions?	Yes (with text field)
	No
Are you currently being treated with any antipsychotic drugs (e.g. Chlorpromazine or Haloperidol)?	Yes
	No
Do you have a history of substance misuse (or substance abuse), or currently have issues relating to substance misuse (or substance abuse)?	Yes
	No

	Prefer not to say
Do you have a history of, or current diagnosis of: psychosis, bipolar disorder, Parkinson's, dementia, or Alzheimer's disease?	Yes
	No
If you answered 'Yes' to the above question, which current diagnosis do you have?	Text Input
Do you have any history of Traumatic Brain Injury (TBI)?	Yes
	No
Do you have any eye disorders, such as: retinal blindness, cataracts, retinal diseases of the eye, or glaucoma? This does not include wearing glasses or contact lenses.	Yes
	No
If you answered 'Yes' please give some more detail about the eye disorder you have.	Text Input
Do you regularly use light therapy, including the use of light boxes, light visors and dawn simulation lamps? This does not include the use of SAD (Seasonal Affective Disorder) alarm clocks.	Yes
	No

33. PLANS FOR COLLECTION, LABORATORY EVALUATION, AND STORAGE OF BIOLOGICAL SPECIMENS FOR GENETIC OR MOLECULAR ANALYSIS IN THE CURRENT TRIAL AND FOR FUTURE USE IN ANCILLARY STUDIES, IF APPLICABLE

This is not applicable to this research study.