Micro-dosing trial protocol

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Over the next year, I am going to conduct a cross-over trial of LSD micro-dosing with an N of one (me), cross-over periods of 40 days, and one-week wash-out between periods. Periods of 40 days balance the risk of carry-over effects against the overall length of the trial. Seven psycho-social outcomes will be assessed. This brief protocol outlines the design and conduct of the trial.

Randomization and administration

An assistant will help me with the randomization. At the start of the experiment, he will be given four empty opaque film canisters marked 'A', 'B', 'C', and 'D', a small bag, two 100μg tabs of LSD, and two 'dummy' tabs of plain paper. He will place the canisters in a bag, draw two at random, and add a tab of LSD[1]. The other canisters will have dummy pieces of paper added.

The canisters will be returned to me in the bag. I will draw one canister which will be 'discarded' (the letter will be noted and the canister will not be used until the next randomization. Removing one canister lessen the sense I will have that the treatment condition is changing between cross-overs). The remaining canisters will then be used in the order drawn from the bag. At the start of each period I will take the relevant canister and add 11mL of distilled water. The lids of the canisters will be cut so that water can be added or extracted without seeing inside. I will leave he canister containing the water in the fridge for at least 5 days.[2].

Every four days I will draw 1ml from the canister and put it in my mouth for 120 seconds before swallowing. After 40 days I will wait a week and then start the next canister. After three-times-40 days, I will give the canisters back to the assistant with new 100μg tabs of LSD to repeat the procedure.

[1] The letters drawn should probably be noted somewhere safe. Note that we are randomizing in blocks of four to ensure that there is variability in the treatment.

[2] The shelf-life of dissolved LSD is difficult to determine but to avoid dosing with expired solution it is safer to generate a new batch at the start of each cross-over

Schedule

The schedule has been updated because of delays in getting started. Since it will be easier to meet with the assistant on Mondays, some of these dates have been shifted slightly from a strict 40-7-40-7 etc. The assessment will be on Tuesday evenings, for consistency:

Figure 1: Practice canister and pipette.

- June 18: Complete baseline outcome measures and enter scores into Google Doc.
- June 19: Start Period 1. First micro-dose of 10 doses every 4 days.
- July 30: First follow-up data collection
- August 5: Start Period 2.
- September 10: Second data collection
- September 16: Start period 3
- … and so on for a total of 9 periods (approximately one year)

Outcome measurement

Seven outcomes will be measured, these are: happiness (Fordyce Emotions Questionnaire), depression (CES-D Questionnaire), work-life satisfaction (Work-Life Questionnaire), flourishing (PERMA), meaning (Meaning In Life Questionnaire), compassion (Compassionate Love Scale), and attachment (Close Relationships Questionnaires). These will all be assessed using tools from the University of Pennsylvania Authentic Happiness project.[3]

The seven outcomes will be measured at baseline and at the end of each 40-day period. The assessment will be self-administered using the online tools in the evening. After completing the assessment I will enter the results into a Google Sheet using a form.

Analysis

The analysis will primarily rely on visual interpretation of charts and inspection of the raw data (i.e. little reliance on statistics to summarise). For example, I will show the medians of the outcomes for each arm (e.g Fig. 1).

To provide evidence about the likelihood that the observed difference between the outcomes associated with each arm occurred by chance, I will use permutation tests. Permutation tests re-assign the data to different arms and compares the distribution of permuted effects with the observed effect. The effect I will use is the differences in the outcome observed; an example of the figure this will produce is shown in fig. 2.

Risks

A pilot delivery of the intervention was completed towards the end of 2018 and no adverse events were observed. Risks will be minimized by close monitoring from friends and family.

[3] `https://www.authentichappiness.sas.upenn.edu/testcenter`

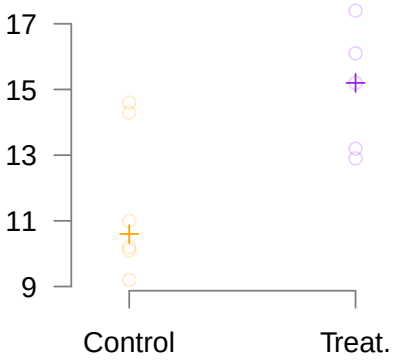

Figure 2: Median of the outcomes in each arm (+), with period-specific results faded.

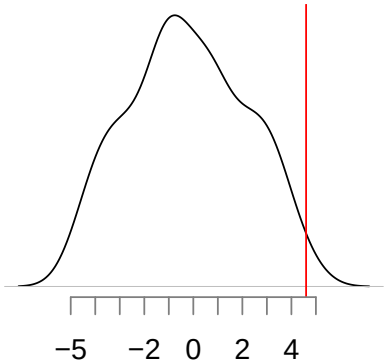

Figure 3: Permutation test results, showing the kernel-density of the permuted differences, and the observed difference as a red vertical line.