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# The altered state of consciousness induced by Δ9-THC

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ABSTRACT

Altered states of consciousness (ASC) provide an opportunity for researchers to study the neurophysiological basis of changes in phenomenal experience. **Δ**9-tetrahydrocannabinol (THC) is the primary psychoactive constituent of cannabis, however whether the effects of THC include ASC features that are shared with other ASC induction mechanisms, such as classical psychedelics, has not been systematically addressed. We used survey (11D-ASC; State Mindfulness), self-report, and natural language processing (NLP) to assess 7.5 and 15 mg oral THC, relative to placebo, in 25 healthy, infrequent cannabis users. THC dose-dependently increased measures of ASC including Insightfulness, and increased ratings of mindfulness and mind-wandering. THC also increased language entropy as previously reported for LSD. Future studies may seek to determine whether reports of increased mindfulness or insight after THC are primarily representative of a psychotomimetic state (i.e., delusional thinking) or conversely, reflect an enhancement of conscious awareness that may be validated empirically.

## 1. Introduction

Altered states of consciousness (ASC) represent an acute and marked deviation in subjective experience from normal/waking consciousness (Dittrich, 1998; Studerus et al., 2010). ASC arise through diverse induction mechanisms including psychoactive drugs, breathing and meditative techniques, or sensory deprivation. Despite these differences, ASC contain shared features or characteristics (Schmidt & Berkemeyer, 2018; Studerus et al., 2010; Watts, 1968). Therefore, the experimental induction of ASC has become a topic of interest in the field of cognitive neuroscience toward relating changes in phenomenological states to underlying biophysical mechanisms (Schmidt & Berkemeyer, 2018). The identification of neurobiological substrates underlying both health (e.g., mindfulness) and disorder (e.g., psychosis) is an important goal for neuroscience and psychiatry.

Δ-9 tetrahydrocannabinol (THC), the primary psychoactive constituent of cannabis, is one compound that may reliably induce ASC (Earleywine et al., 2021; Zaytseva et al., 2019). Despite shifts in the global policy landscape related to cannabis use, very little is known empirically about the nature of subjective effects induced by cannabis or THC, including which effects may be mediated by THC alone or THC in combination with other compounds within the cannabis plant (LaVigne et al., 2021; Morgan et al., 2018). Case reports on the subjective effects of cannabis have detailed robust alterations of cognition and perception (Barrett et al., 2018; Keeler et al., 1971; Perna, 1969) resulting in early classifications for cannabis as a “hallucinogen” (Keeler et al., 1971). Specifically, early questionnaires probed respondents for alterations that had occurred “while under the influence of marijuana.” 90% of respondents endorsed seeing

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"colors or objects as more intense," ~50% endorsed "hallucinating colors or designs" and about a third "felt closer to God, nature, mankind, or felt better able to understand the meaning of the universe." (Keeler et al., 1971). More recent placebo-controlled studies in laboratory settings have found that the magnitude of subjective effects elicited by THC alone are roughly comparable to those elicited by cannabis containing the same doses of THC (Wachtel et al., 2002).

In the brain, THC activates cannabinoid (CB1) receptors predominately expressed throughout the cortex, cerebellum, hippocampus, amygdala and striatum (Mackie, 2005). In these regions, CB1 receptor activation directly regulates the release of inhibitory (GABA) and excitatory (glutamate) neurotransmitters and indirectly regulates the release of neuromodulators including dopamine and serotonin (Araque et al., 2017). Primarily, CB1 receptors regulate the release of GABA from inhibitory interneurons in the cortex, thereby facilitating or disinhibiting excitatory output from projection neurons to activate brain regions (Fortin et al., 2004; Kiritoshi et al., 2016; Kovacs et al., 2012). Neuroimaging studies consistently show increased cerebral blood flow after THC indicating greater activation of the frontal cortex, insula, and cingulate (for review see (Bloomfield et al., 2019)), brain regions critical for self-awareness, consciousness and cognition (Craig, 2009; de Souza et al., 2014; Hadland et al., 2003; Huang et al., 2021; Miller et al., 2002). Acute THC administration also affects neural networks, including blocking the deactivation of the rest-related default-mode network during intended task engagement (Bossong et al., 2013). THC similarly affects neural oscillations by blocking reductions in the rest-related alpha wave during intended task engagement, analogous to the default-mode network findings (Murray et al., 2022).

Serotonin (5-HT)2A receptor agonists, also known as classical psychedelics, are more often associated with ASC than CB1 agonists (Liechti et al., 2017). The past decade has seen a resurgence of clinical studies with compounds that activate the 5-HT2A receptor, including psilocybin and lysergic acid diethylamide (LSD) (Davis et al., 2021; De Gregorio et al., 2021; Nutt et al., 2020; Tullis, 2021). The subjective effects of these compounds may be instrumental in mediating therapeutic outcomes (Preller et al., 2017; Yaden & Griffiths, 2021), and more broadly, may aid in empirical studies of consciousness (Bayne & Carter, 2018; Yaden & Griffiths, 2021). 5-HT2A receptors are present throughout the cortex, and their activation has been shown to promote diverse network connectivity, or "entropy," across the brain (Carhart-Harris & Friston, 2019; Carhart-Harris et al., 2014) in part through facilitating the release of the excitatory neurotransmitter glutamate from thalamocortical nerve fibers (Aghajanian & Marek, 2000; Beique et al., 2007; Nichols, 2016; Preller et al., 2019). Unlike CB1, 5-HT2A activation impacts all frequency bands of brain waves by reducing the power, or amplitude, of these neural oscillations at rest (Muthukumaraswamy et al., 2013). Notably, this occurs even after the administration of "microdoses" (i.e., 13 and 26 μg LSD) below the threshold of intoxicating effects, yet not after high doses (15 mg) of THC, indicating that broadband reductions in oscillatory power, which may be associated with therapeutic outcomes, are not a necessary biophysical feature of ASC (Murray et al., 2022; Murray et al., 2021). To what extent the phenomenological features of ASC induced by 5-HT2A agonists compare to the CB1 agonist THC is a major aim of the current study.

In addition to 5-HT2A and CB1 receptor systems, ASC may be induced by other pharmacological and non-pharmacological means, including dissociative drugs such as ketamine, entactogens such as 3,4-methylenedioxymethamphetamine (MDMA), continuous exposure to visual and auditory stimulation (Bartossek et al., 2021; Schmidt et al., 2020), or various meditative techniques (Milliere et al., 2018). While some neurophysiological and phenomenological commonalities have been reported between meditative and drug-induced states, including the dissolution of the sense of self (Milliere et al., 2018), the variety of meditation techniques and contemplative practices makes broad generalizations here difficult. For an in-depth review of the neurobiology and phenomenology of meditative states as compared to classical psychedelics, see work by Millere and colleagues (Milliere et al., 2018).

How are ASC phenomena studied? In recent years, researchers have developed systematic approaches to evaluate the features of ASC across induction mechanisms. These approaches include psychometrically validated questionnaires and natural language processing (NLP) of speech or text content generated during ASC. The present study leverages both approaches, examining THC ASC through the lens of closed-ended questionnaires and open-ended self-reports. One questionnaire that has gained prominence in recent years is the altered states of consciousness rating scale (11D-ASC). The 11D-ASC comprises 11 dimensions or subscales including Experience of Unity, Complex Imagery, and Insightfulness (Studerus et al., 2010). This questionnaire was developed to test the hypothesis that ASC contain shared features, independent of their means of induction, toward a taxonomy of ASC. Studies with the 11D-ASC have shown that compounds including psilocybin, ketamine, and MDMA, and non-pharmacological techniques involving sensory stimulation, are indeed sensitive to the subscales (Carbonaro et al., 2018; Kometer et al., 2012; Liechti et al., 2017; Pokorny et al., 2017; Preller et al., 2016; Schmidt & Prein, 2019), with some expected differences in the magnitude of subscale ratings. For instance, ketamine is highly sensitive to Disembodiment, whereas MDMA is highly sensitive to Blissful State, and psilocybin to Elementary Imagery. To date, the 11D-ASC has not been used to assess ASC during meditation, although reports from meditative-like states, including autogenic training, were used in the development of the questionnaire (Dittrich, 1998).

The 11D-ASC enables a detailed assessment of ASC, however, it is not designed to be exhaustive, or encompass all features that may accompany ASC. Thus, the current study employs two complementary rating scales, one assessing mind-wandering, and the other, mindfulness, in addition to NLP assessments of open-ended self-report. Mind-wandering is assessed with a 1–10 rating scale administered immediately following a behavioral task, such as a working memory task. Increases in mind-wandering are related to decreases in task performance. The level of mind-wandering after drug administration, or during meditative states, is dependent on both drug type and meditation technique (Adam et al., 2020; Milliere et al., 2018). Rating scales have also been developed to assess states and traits of mindfulness. The state of mindfulness generally refers to a state of greater awareness of one's sensations, emotions, and thoughts, with a non-judgmental attitude. In our analysis, we used the State Mindfulness Scale, designed to capture both traditional Buddhist and contemporary scientific models of mindfulness (Tanay & Bernstein, 2013). To our knowledge, only one study has explored changes in state mindfulness after drug administration, finding non-significant increases after psilocybin (315 μg/kg; oral) (Smigielski et al., 2019).

Complementary to psychometric questionnaires, natural language processing enables an analysis, not only of the content of ASC, but also of how that content is expressed through language. These analyses might help identify shared features between drug effects and states of mental health or disorder to guide diagnoses and treatments (Tagliazucchi, 2021). NLP has been used to quantitatively evaluate open-ended self-reports after classical psychedelics including LSD, psilocybin, ayahuasca, and N,N-dimethyltryptamine (DMT), in addition to MDMA, ketamine, and antidepressants (Hase et al., 2022; Sanz et al., 2021). In a large dataset of available online reports (N = 2947), relative to antidepressants, language content after MDMA was highly emotional, whereas Ayahuasca and DMT linguistic markers were highly associated with mystical experiences. In placebo-controlled studies with MDMA (1.5 mg/kg), MDMA resulted in greater semantic proximity to the concepts of friend, support, intimacy, and rapport (Bedi et al., 2014) and an increase in use of social and sexual words (Baggott et al., 2015). In a placebo-controlled study examining LSD's effects on language, Sanz and colleagues identified increases in the entropy of verbally communicated topics, which paralleled prior findings of greater neural entropy after LSD (Sanz et al., 2021). To our knowledge, NLP has not been applied to cannabis or THC intoxication, or to non-pharmacological techniques of ASC induction, including acute meditative states.

The purpose of our study was to examine the subjective effects of THC through surveys and natural language to enable a "window into the intoxicated mind" (Baggott et al., 2015; Bedi et al., 2014) and facilitate comparison with 5-HT2A receptor agonists through a CB1 receptor-based ASC induction mechanism. Our central hypothesis was that THC induces ASC that mimic classical psychedelic states. Here, we assessed the acute effects of THC (7.5 and 15 mg) vs placebo in healthy men and women that were not regular cannabis users and with little to no prior experience with classical psychedelic substances. Ratings of mind-wandering and written self-reports of THC or placebo effects were collected near the anticipated peak drug effect. Ratings of mindfulness and altered states of consciousness were collected retrospectively at the end of sessions. NLP was performed on text transcribed from written self-report and included measures of language entropy, sentence perplexity, and classification to predict THC or placebo reports. This work is a sub-analysis of a larger study that included behavioral and neurophysiological assessments in the same set of participants, with one additional participant included here that did not participate in the neurophysiological measures (Murray et al., 2022).

## 2. Methods

### 2.1. Study design

Healthy adults (N = 25) participated in three 5-hour sessions in which they received capsules containing THC (7.5 or 15 mg) or placebo. THC was administered under double-blind and randomized conditions. Dependent measures included surveys of mind-wandering, state mindfulness (SMS), altered states of consciousness (11D-ASC), and natural language processing of self-reported effects.

### 2.2. Subjects

Participants (N = 25) were healthy adult males and females (either aged 18–20 or 30–40 years) who had used cannabis 1–20 times in their lifetime but had not used the drug in the last 30 days (Murray et al., 2022). Participants were recruited through local advertisements in social media platforms (Instagram, Facebook) and through paper flyers. Advertisements included links to intake surveys to determine initial eligibility in the study, and to provide contact information. A negative urine test for THC was required at each session. They were screened for physical and psychiatric health with a physical examination, electrocardiogram, modified Structural Clinical Interview for DSM-5, and self-reported health and drug-use history. Inclusion criteria were English fluency, right-handedness, at least a high school education and body mass index of 19 to 26 $kg/m^2$. Exclusion criteria included a history of psychosis, severe posttraumatic stress disorder or panic disorder, past-year substance use disorder (except nicotine), pregnant or nursing, working night shifts, and regular medication aside from birth control.

### 2.3. Orientation session

Prior to experimental sessions, subjects reviewed the protocol, provided informed consent, received presession instructions, and practiced study tasks and questionnaires. They were instructed to abstain from alcohol for 24 h and other recreational drugs for at least 2 days before each session. They were permitted to consume their normal amounts of caffeine and nicotine up to 3 h before sessions. Subjects were instructed to have a normal night's sleep and fast for 12 h before the sessions. A granola bar was provided at arrival as a standardized breakfast. To minimize drug-specific expectancies, subjects were told they might receive a placebo, stimulant, sedative, or cannabinoid drug. Subjects provided informed consent prior to beginning the study procedures.

### 2.4. Ethics committee approval

Study procedures were approved by the University of Chicago Institutional Review Board. Subjects provided informed consent to study procedures during the orientation session.

### 2.5. Experimental sessions

Subjects attended three 5-hour sessions from 9 am to 2 pm, separated by at least 7 days. Compliance to drug abstention was verified by urinalysis (CLIAwaived Instant Drug Test Cup, San Diego, CA) and breath alcohol testing (Alcosensor III, Intoximeters, St. Louis, MO). Female subjects provided urine samples for pregnancy tests and were tested at any phase of the menstrual cycle. After compliance tests, pre-drug measures of subjective state were obtained, and THC (7.5 or 15 mg) or placebo was administered orally under double-blind conditions. Subjective measures were taken at 60, 90, 120, 180, and 240 min, and written self-reported effects were obtained near peak drug effects at 100 min. After written self-report, participants rated their degree of mind-wandering during a working memory task. Other behavioral tasks were also administered during this time, followed by neurophysiological measures with electroencephalography. Methods and results of the behavioral and neurophysiological assessments have been previously published (Murray et al., 2022). Following the final time point at 240 min, subjects completed an end-of-session questionnaire and were discharged.

### 2.6. Drug

THC (Marinol® [dronabinol]; Solvay Pharmaceuticals; 7.5 mg and 15 mg) was placed in opaque capsules with dextrose filler. Placebo capsules contained only dextrose. The 7.5 and 15 mg doses reflect the amount of THC in one-quarter or one-half of a cannabis cigarette containing 0.2 g of 15% THC, respectively. These doses of THC are known to produce performance impairments as well as subjective intoxication (Broyd et al., 2016; Hartman & Huestis, 2013; Pabon & de Wit, 2019).

### 2.7. Self-report

Subjective drug effects were assessed during sessions before and at regular intervals after drug administration using a 12-item, true/false ARCI Marijuana scale specific to cannabis effects. Specific items include “I have an increasing awareness of bodily sensations” and “My thoughts seem to come and go” (Haertzen et al., 1963; Martin et al., 1971). The KR-20 reliability coefficient for the ARCI Marijuana scale is 0.77 (Haertzen et al., 1963). During sessions, near peak drug effects (100 min), participants rated levels of mind-wandering during a working memory N-back task (Gevins & Cutillo, 1993) from 1 “not at all” to 10 “almost always.” The mind-wandering assessment was administered immediately after the N-back task. During the task, participants responded when the current visual and audio stimulus (a letter) was the same as the one presented 1, 2, or 3 trials earlier. Also during this time of peak drug effects, participants provided a written self-report, wherein they were instructed to “Attend to your experience in the moment, and write as little or as much as you like about any thoughts or sensations you’re having for the next 10 min.” Measures of natural language processing were applied on these written self-reports. At the end of each session, subjects completed an end-of-session questionnaire comprised of the Dimensions of Altered States of Consciousness (11D-ASC) questionnaire (Dittrich, 1998). The 11D-ASC consists of 11 subscales indexed from 94 individual visual analog items rated from 0 to 100. Cronbach’s alpha, a measure of internal consistency, ranged from 0.73 to 0.91 across the 11 subscales (Studerus et al., 2010). Also at session end, subjects completed the State Mindfulness Scale (Tanay & Bernstein, 2013), consisting of 21 items (15 items for mindfulness of mind, 6 for mindfulness of body) rated from 1 “not at all” to 5 “very well.” Cronbach’s alpha for the mindfulness of mind and body subscales were found to be 0.95 and 0.89 respectively.

### 2.8. Natural language processing

#### 2.8.1. Semantic entropy

Semantic analysis was conducted using a Word2Vec (Mikolov et al., 2013) model pre-trained with the Google News corpus (https://news.google.com/), comprising a vocabulary size of $\simeq 3^6$ unique words using the skip-gram neural network architecture with dimension 300, a commonly used framework for such measures. Word embedding models such as word2vec work on the principle of *distributional semantics,* that words that are used and occur in the same contexts tend to have similar meanings. Vectors of words that represent similar concepts would be located close to each other in this high dimensional space, allowing us to measure between words to identify how close they are to each other. We use the word embedding model to assign vector representations to each of the words recorded by the participants. We measure the semantic distance between words by measuring the cosine of the angle between their respective vectors in the embedding, i.e. $d(u, v) = 1 - u.v / ||u||\ ||v||$, for two vectors u and v. The semantic distances of consecutive words were computed, and for each sentence, we averaged the semantic distance. We then used this measure to serve as a metric of semantic coherence in texts. A high average value of semantic distances implies that some consecutive words were far apart in the vector embedding, and that more semantically diverse concepts were explored. Such a measure has been used previously to identify natural language disorganization during altered states of consciousness (Sanz et al., 2021).

#### 2.8.2. Color entropy

Color entropy, like semantic entropy, is a measure of language entropy. We used multiple measures of language entropy to capture the multi-modal nature of language (Bergen, 2012). Color entropy operationalizes the entropy of words based on their color associations or relationships (i.e., banana and apple have greater entropy than banana and lemon). Color relationships in words were determined with Word-to-Color vectors and assessed for entropy within sentences. Specifically, every word was mapped to an 8-dimensional color vector that encodes the average color distribution of 100 images associated with the word. These vectors have previously been used to identify clustering in abstract semantic domains, as well as classify between metaphorical and literal word pairs (Desikan et al., 2020; Guilbeault et al., 2020). Sentences with a high semantic entropy do not necessarily have high word-color entropy, as each of these representations captures different aspects of word meaning. We use color entropy in addition to distributional semantics to account for embodied, multi-modal language meaning and its subsequent disorganization.

### 2.8.3. Language model sentence perplexity

Perplexity is a linguistic measure that quantifies the unlikelihood of a sentence and has been used to study dementia in Alzheimer's patients (Cohen & Pakhomov, 2020). Sentences that are more probabilistically likely are given a lower score on this measure (Miaschi et al., 2021; Wang et al., 2019). Perplexity is mathematically defined as the exponentiated average negative log-likelihood of a sequence. If we have a tokenized sequence X= (x0, x1, …, xt), then the perplexity of X is,

$$PPL(X) = \exp\left\{ -\frac{1}{t}\sum_{i}^{t} \log p_\theta(x_i|x_{<i}) \right\}$$

where logpθ(xi|x < i) is the log-likelihood of the ith token conditioned on the preceding tokens x < i according to our model. We used the GPT-2 (Radford et al., 2019) and BERT (Devlin et al., 2018) language models to calculate our perplexity scores for the sentences.

### 2.8.4. Topic models and word clouds

Topic models (Blei & Lafferty, 2009) are probabilistic graphical models that represent collections of textual documents from underlying latent topics. These allow us to see if there are words that tend to appear around each other more often, and together, form a latent topic. We used a Latent Dirichlet Allocation (LDA) (Blei et al., 2003) topic model with two topics on the dataset of participants' sentences. Frequent word associations with topics were also presented in the form of word clouds. The size of the words corresponds to the prevalence of the word in the topic.

### 2.8.5. Classifying placebo vs drug

Text classification models were used to predict which class a body of text belongs to based on its textual features. Classes included placebo and drug groups. Text data were preprocessed by word tokenization, removal of stop words, and converted to Term Frequency Inverse Document Frequency format (TF-IDF). TF-IDF enables representation of words and their relative importance in the whole text corpus and individual document. After preprocessing, text classification was applied with Support Vector Machine using a Doc2Vec (Le & Mikolov, 2014) embedding. Doc2Vec semantically embeds each document in a high-dimensional space. We then visualized this Doc2Vec representation in a low dimensional space using Uniform Manifold Approximation and Projection (UMAP) (Leland et al., 2018).

## 2.9. Statistical analysis

ARCI Marijuana: Within-session responses were assessed with RM-ANOVA using time and dose as within-subject factors. 11D-ASC, mind-wandering, and State Mindfulness scales: For each measure, 7.5 and 15 mg THC were compared against placebo in separate RM-ANOVAs using dose as within-subjects factor. Natural Language Processing: Entropy and Perplexity measures were calculated for each subject. RM-ANOVAs with dose as within-subjects factor were used for each measure. For all RM-ANOVA, if significant linear effects of dose were found, follow-up planned contrasts compared each THC dose to placebo. Bonferonni adjusted p values were used to correct for multiple comparisons in measures containing subscales. All statistical analyses were conducted with SPSS (Version 25; IBM Corporation, Armonk, NY).

**Table 1**
Demographics and drug use characteristics.

| Category | *n* or Mean ± SD (Range) |
|---|---|
| Subjects (Male/Female) | 25 (12/13) |
| Age, Years | 25.2 ± 6.6 (18–34) |
| Body Mass Index, kg/m$^2$ | 23.1 ± 2.4 (19.5–26.6) |
| Weight, lbs | 152.1 ± 22.7 (101–189) |
| Race | |
| Caucasian | 13 |
| African American | 2 |
| Asian | 1 |
| Other/>1 Race | 9 |
| Current Drug Use | |
| Cannabis, months since last use | 5.2 ± 7.4 (1–24) |
| Alcohol, drinks/week ($n = 6, 10$) | 3.1 ± 3.3 (0–11) |
| Alcohol, drinking days/week | 1.4 ± 1.6 (0–6) |
| Tobacco, times/week ($n = 1, 2$) | 0.3 ± 1.0 (0–5) |
| Caffeine, servings/day ($n = 11, 11$) | 0.8 ± 0.7 (0–2) |
| Total Lifetime Drug Use, Nonmedical | |
| Cannabis ($n = 12, 12$) | 12.0 ± 6.8 (1–20) |
| Classical Psychedelic ($n = 3, 5$) | 0.8 ± 0.3 (0–6) |
| MDMA ($n = 0, 2$) | 0.2 ± 0.6 (0–2) |
| Stimulant ($n = 2, 2$) | 0.4 ± 1.1 (0–5) |
| Opiate ($n = 0, 0$) | 0 |

## 3. Results

### 3.1. Demographic characteristics

Participants were 25 years of age on average and reported minimal current or prior substance use. In addition to meeting inclusion criteria of <20 total lifetime cannabis use and 0 use in the last 30 days, participants reported an average of 5 months since last cannabis use, and less than one lifetime or total classical psychedelic experience (Table 1).

### 3.2. Self-report measures

On subjective ratings, both doses of THC (7.5 and 15 mg) increased ratings of marijuana-like effects (ARCI Marijuana) over the course of sessions (Fig. 1A) (main effect of dose: $F_{1,24} = 54.68$; $p < 0.001$; time $F_{1,24} = 55.80$; $p < 0.001$; and dose × time interaction: $F_{1,24} = 38.96$; $p < 0.001$). During peak drug effects, THC dose-dependently increased ratings of mind-wandering during the working memory task (Fig. 1B) ($F_{1,24} = 33.28$; $p < 0.001$). At session end, participants retrospectively reported on mindfulness and altered states of consciousness. THC dose-dependently increased mindfulness of mind and body (State Mindfulness Scale) (Fig. 1C) (mind:

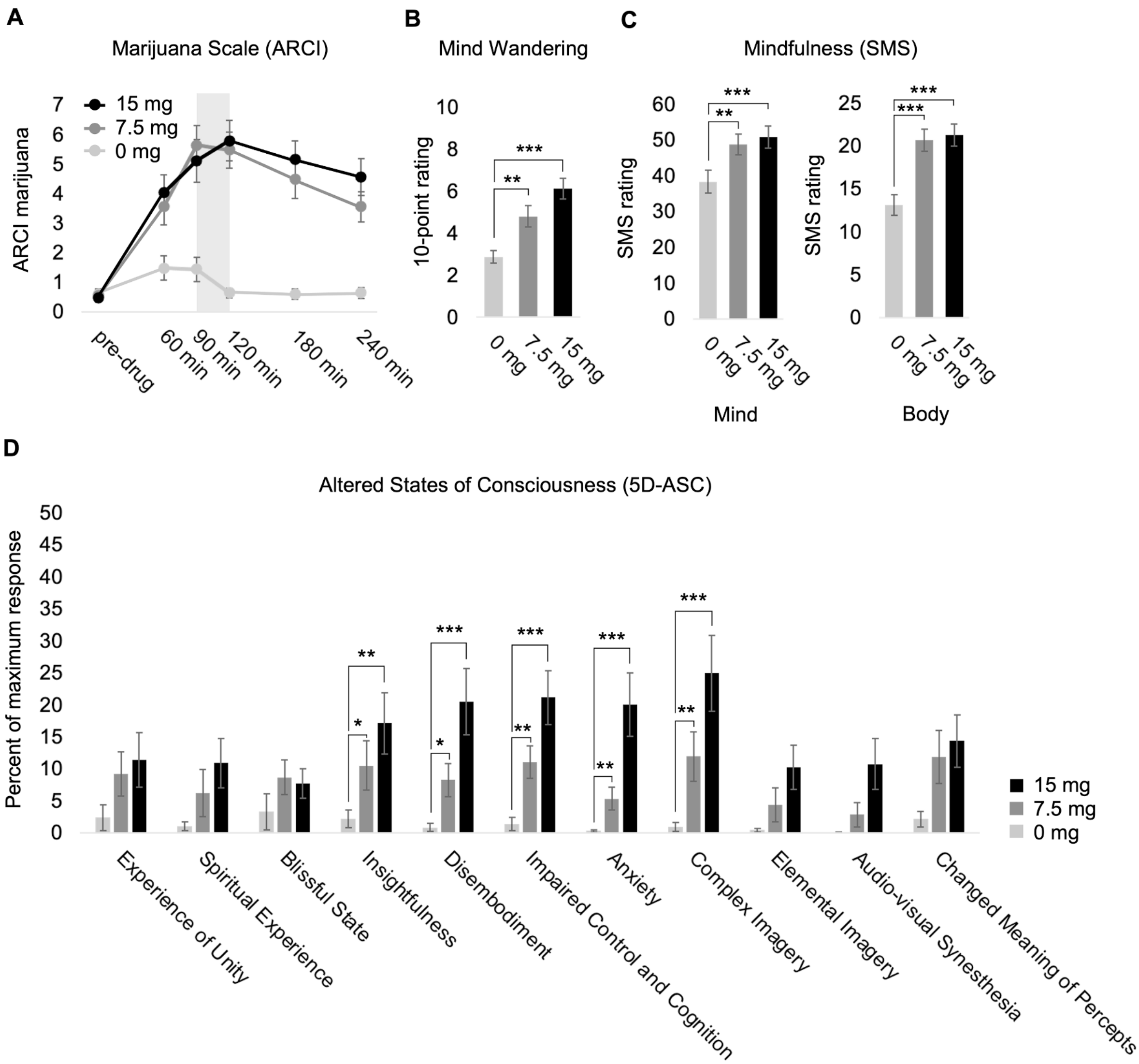


**Fig. 1.** Survey responses after 0, 7.5, or 15 mg THC; data expressed as mean ± SEM. Time course of THC effects across study sessions indexed by the ARCI Marijuana scale (A); shaded region indicates period that tasks were administered, including mind-wandering and written self-reports. Mind-wandering reports after working memory task (B). Retrospective (end-of-session) ratings of state mindfulness of mind (Mind) and body (Body) (SMS; State Mindfulness Scale) (C). Altered states of consciousness subscales (11D-ASC) (D). Repeated-measures ANOVA resulted in significant main effects of dose ($p < 0.05$) for all surveys. Follow-up independent t-tests compared each THC dose to placebo (*p < 0.05; **p < 0.01; ***p < 0.001).

$F_{1,24} = 18.601$; $p < 0.001$; body: $F_{1,24} = 45.82$; $p < 0.001$) and dose-dependently increased ratings on all but two of the 11 subscales of altered states. Subscales included Insightfulness ($F_{1,24} = 10.49$; $p = 0.003$), Disembodiment ($F_{1,24} = 15.98$; $p = 0.001$), Impaired Control and Cognition ($F_{1,24} = 23.32$; $p < 0.001$), Anxiety ($F_{1,24} = 15.64$; $p = 0.001$), and Complex Imagery ($F_{1,24} = 17.05$; $p < 0.001$) (Fig. 1D).

### 3.3. Natural language

Text data were transcribed from participants' written self-reports near peak THC effects for natural language processing. Qualitatively, written reports included depictions of alterations in self, time perception, visual perception, and cognition. Quotes include: *"Things appear larger the longer I stare at them"; "time is confusing"; "the interface between me and me… the behaving me, the observing me."* Prior to machine learning analyses, we assessed word counts across drug conditions. THC (7.5 or 15 mg) did not affect the number of written words during the 10-minute reporting sessions (Mean ± SD; Placebo: 71.08 ± 57.72; 7.5 mg THC: 71.00 ± 44.58; 15 mg THC: 71.24 ± 43.13;). This lack of change in total word counts enabled direct comparison of text across drug conditions in our following analyses of natural language.

We analyzed natural language across placebo, 7.5 mg THC, and 15 mg THC using two language entropy measures and one measure of sentence perplexity (Fig. 2). THC dose-dependently increased color, but not semantic entropy (Fig. 2A,B) ($F_{1,24} = 4.40$; $p = 0.046$). THC effects also trended toward increased sentence perplexity, but this was not statistically significant (Fig. 2C). We then combined reports across drug conditions to explore text content using topic modeling with the choice of two topics. Topic modeling revealed associations of words along two topics that largely represented the placebo and THC groups. From these words, we created word clouds, which allowed us to see how these topics represented the groups. The words "feel", "little", "tired," "yesterday" and "breakfast" appeared frequently in topic 1 (representing placebo-related effects), while words "time", "moving", "weird", "drug", and "embarrassed" appeared frequently in topic 2 (representing THC-related effects) (Fig. 3A). Finally, we assessed text content with machine learning classification. Our classification model found that the textual content served as a strong predictor of whether content belongs in placebo or THC groups, with classification accuracies of 87.5% (Support Vector Machine on Doc2Vec embedded data) (Fig. 3B; Supplementary Fig. 1).

## 4. Discussion

Our goal was to investigate the subjective effects of oral THC in infrequent cannabis users to determine whether these effects include features of altered states of consciousness that are characteristic of other ASC induction mechanisms, including classical psychedelics. We found that THC dose-dependently increased most subscales of the 11D-ASC in addition to increasing language entropy, findings that have been reported after LSD and psilocybin (Kometer et al., 2015; Liechti et al., 2017; Sanz et al., 2021). THC also dose-dependently increased ratings of both mind-wandering and mindfulness. Our findings inform the nature of subjective effects of THC and role for CB1 receptor-dependent signaling in the modulation of consciousness and cognition.

THC effects on the 11D-ASC were similar to classical psychedelics (Gouzoulis-Mayfrank et al., 2005; Kometer et al., 2015; Liechti et al., 2017; Schmidt & Berkemeyer, 2018) and ketamine (Studerus et al., 2010), with many, but not all 11D-ASC subscales affected by

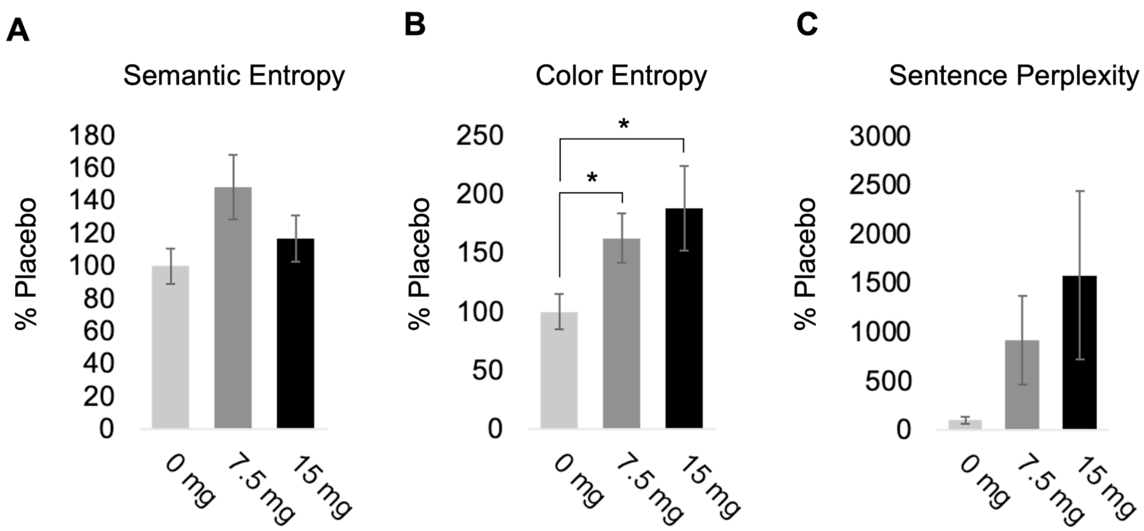


**Fig. 2.** Natural language processing measures on text transcribed from 10-min written self-reports after 0, 7.5, or 15 mg THC; data normalized to placebo (0 mg) and expressed as mean ± SEM. Semantic Entropy (A). Color Entropy (B). Sentence Perplexity (C). Repeated-measures ANOVA resulted in significant main effect of dose ($p < 0.05$) for Color Entropy. Follow-up independent t-tests compared each THC dose to placebo (*$p < 0.05$).

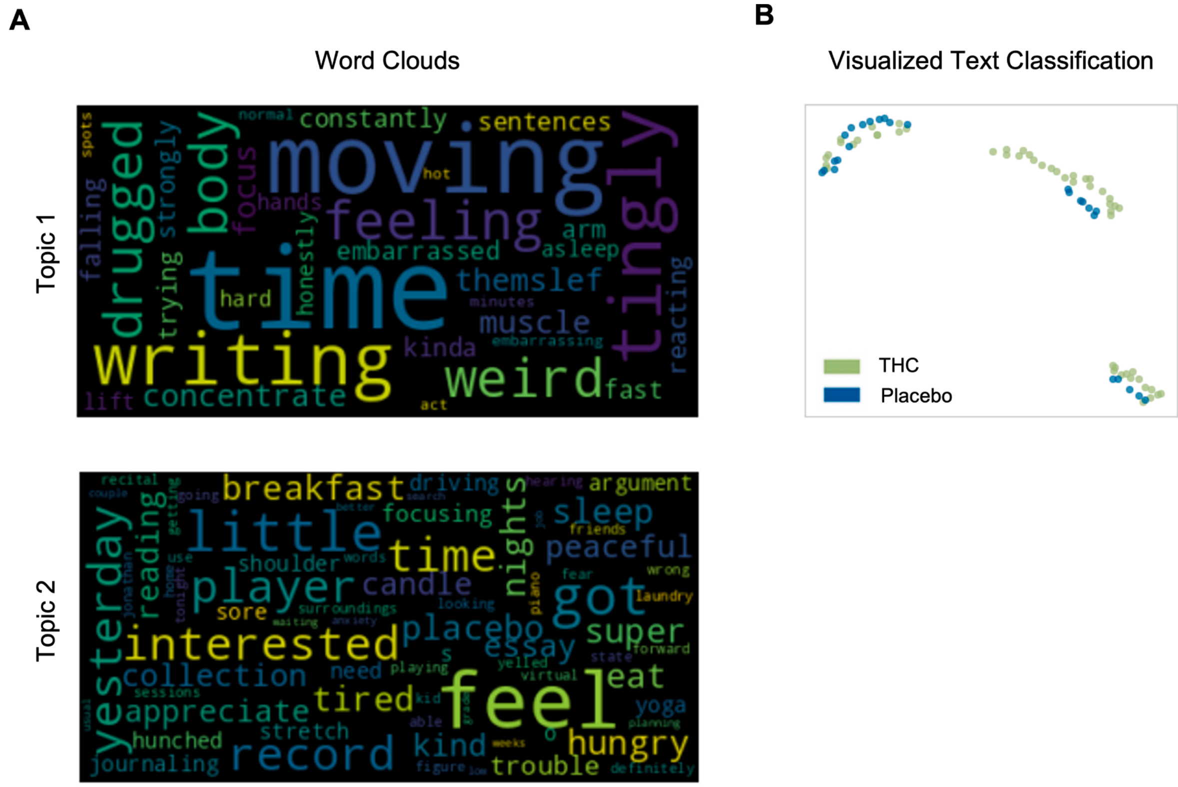


**Fig. 3.** Word clouds associated with two topics derived from topic modeling (A). One topic represented THC-related effects (top); another represented placebo-related effects (bottom). Visualization of classified text (87.5% accuracy using Support Vector Machine on Doc2Vec embedded data) in a semantic space using Uniform Manifold Approximation and Projection (B). The figure shows separation of THC (green) and placebo (blue) texts based on the classification of words, while clusters demonstrate conceptual similarity in the meaning of the words.

THC. One measure that was not affected by THC was Blissful State. We note that Blissful State is a measure that may be sensitive to many substances that do not induce other features of ASC (i.e., stimulants), indicating that THC effects on the 11D-ASC were specific to discrete features of ASC and not representative of increased responding to drug effects in general. Our 11D-ASC findings with oral THC are supported by a recent report that identified neural correlates of subjective responses on the 11D-ASC after smoked cannabis administration (one cigarette of unspecified weight or THC content) (Zaytseva et al., 2019). Our report here indicates that THC (7.5 and 15 mg, oral) is sufficient to induce altered states of consciousness, that is, does not require combinations with minor cannabinoids or terpenes within the cannabis plant known to modulate the effects of THC (LaVigne et al., 2021; Morgan et al., 2018). These data add to the literature indicating that specific subjective effects of THC and cannabis are shared, not only across individuals following THC administration, but across altered state induction mechanisms. Future studies may seek to assess the veracity of Insightfulness reported after THC relative to other ASC inductions mechanisms.

Our finding that THC dose-dependently increased mind-wandering is consistent with a previous report after 15 mg THC (Adam et al., 2020). Mind-wandering has been shown to encompass a broad range of psychological processes (Wang et al., 2018) involving increased creativity (Leszczynski et al., 2017; Smeekens & Kane, 2016) 'Aha!' moments of insight (Gable et al., 2019; Zedelius & Schooler, 2015), and changes in mood states (Mills et al., 2021). In terms of affect, a wandering mind might involve negative thoughts that predict negative moods (Killingsworth & Gilbert, 2010), such as those focused on the past or other individuals (Ruby et al., 2013), whereas wandering thoughts on the future, or self, were shown to predict positive moods (Ruby et al., 2013). Mind-wandering is linked to activity within the default mode network (DMN) (Mason et al., 2007). DMN activity or connectivity is also increased or sustained after administration of THC (Bossong et al., 2013; Cheng et al., 2014; Zaytseva et al., 2019). Conversely, DMN connectivity and mind-wandering were found to be reduced after psilocybin (Carhart-Harris et al., 2012; Polito & Stevenson, 2019), LSD (Carhart-Harris et al., 2016), and ayahuasca (Palhano-Fontes et al., 2015), substances known to activate 5-HT2A receptors. For these classical psychedelics, reductions in DMN connectivity have been suggested to benefit patients with depressive rumination, a maladaptive form of mind-wandering, by reducing DMN-dependent self-referential processing (Carhart-Harris & Friston, 2019). For THC, increases in mind-wandering, alongside DMN connectivity, may be related to self-referential processing.

Increased self-referential processing following THC is supported by our finding that THC dose-dependently increased both mindfulness of mind and mindfulness of body. That is, participants endorsed items related to increased awareness of mental contents and bodily states. To our knowledge, this is the first study to examine or report increases in mindfulness following acute cannabis or THC administration. One study assessing psilocybin effects on mindfulness during a mindfulness retreat failed to detect acute increases in state mindfulness, but did detect increased ratings of mindfulness at 4 months post-intervention (Smigielski et al., 2019). Measures of mindfulness are primarily reported in association with meditative practices. For instance, a 4-day Isha Yoga retreat increased ratings of mindfulness that were associated with increased levels of blood endocannabinoids (the endogenous signaling molecules which activate CB1 receptors in the brain) (Sadhasivam et al., 2020). Specifically, the endocannabinoids 2-AG and anandamide were correlated with happiness and well-being after the retreat. In that study, participants with over 20% increases in 2-AG also showed greater increases in mindfulness. Based on these data, the authors of that report, Sadhasivam and colleagues, suggest that endocannabinoids may be a biomarker of meditation. By extension, their work supports the notion that THC, an exogenous cannabinoid, may facilitate meditative states. Meditation techniques vary greatly however, and those that fall under 'mindfulness meditation' are largely split between two main practices known as focused attention and open monitoring, each of which have separate aims and neural correlates (Lutz et al., 2008). Focused attention involves sustaining attentional focus on an object or breath with an aim of gaining control over and reducing mind-wandering, and thus, is associated with reductions in DMN function (Brewer et al., 2011; Farb et al., 2007; Lutz et al., 2016; Scheibner et al., 2017). Open monitoring involves a receptive observation of the mental contents in the present moment and is related to activation in anterior insula, anterior cingulate and somatosensory cortices (Kuzbiel, 2018; Lutz et al., 2008). THC frequently activates insular and cingulate cortices (Bloomfield et al., 2019) and fails to reduce DMN function (Bossong et al., 2013; Cheng et al., 2014; Zaytseva et al., 2019), drawing closer comparisons to open monitoring than focused attention practices on both neurobiological and phenomenological measures.

To further examine the altered state induced by THC, we used NLP measures on written self-reports of THC effects. These NLP measures covered multiple aspects of language organization to reflect the multi-modal nature of language (Bergen, 2012; Lakoff & Turner, 2009). We included two language entropy measures, one for words based on distributional semantics and another based on color-associated information to capture multi-modal entropy (Desikan et al., 2020; Guilbeault et al., 2020). We found that THC increased color entropy, but effects on semantic entropy were not significant. Our finding of increased language entropy is consistent with a previous report after administration of 75 μg LSD. Specifically, Shannon's information entropy increased alongside increased semantic variability (Sanz et al., 2021).

What does greater language entropy mean for mental health? The effects of both cannabis and classical psychedelics have drawn comparisons to psychosis, resulting in the "psychotomimetic" label for these drugs (Nichols & Walter, 2021). Our data contribute to comparisons to psychosis made through natural language. Increases in language entropy, including speech disorganization and reduced semantic coherence have been reported in patients with schizophrenia (Bedi et al., 2015; Corcoran et al., 2018; Elvevag et al., 2007; Marggraf et al., 2018; Spencer et al., 2021). Early studies also demonstrated that classical psychedelics enhance free-association or render speech less predictable (Amarel & Cheek, 1965). Interestingly, these findings in language entropy extend to neural activity. Increases in neural entropy, measured by Lempel-Ziv Complexity (LZP) during resting-state, have been reported after intravenous THC (Cortes-Briones et al., 2015), LSD, psilocybin and ketamine (Schartner et al., 2017), and in patients with schizophrenia (Xiang et al., 2019). In the THC study, increased neural entropy correlated with psychosis-like positive symptoms and thought disorganization symptoms. However, health benefits may accompany psychotomimetic risks. LSD-induced entropic brain activity predicted positive personality changes 2 weeks after treatment, indicating that acutely, entropic states may target rigid behavioral patterns for enduring positive outcomes (Lebedev et al., 2016).

The current study was not without limitations. This study was a subset of a larger study, which assessed neurophysiological effects of THC (Murray et al., 2022). In that study, we found that unlike LSD or psilocybin (Carhart-Harris et al., 2016; Kometer et al., 2015; Muthukumaraswamy et al., 2013), THC did not induce broadband reductions in neural oscillations. One limitation of the current report is that additional neurophysiological measures were not included, such as THC's potential effects on neural entropy, which might have informed the relationship between brain states and altered states of consciousness. Related to this point, the current report was limited by the measures included to assess an overall picture of ASC after THC. Additional questionnaires that operationalize beneficial effects such as psychological insight, or detrimental effects such as positive psychotic symptoms, would have provided a more complete picture. Similarly, while we were selective with our NLP measures prior to analysis, we note that a variety of NLP measures could have been applied to our data, including sentiment analysis. Sentiment analysis could have informed whether the ASC experience after THC accompanied positive, negative, or neutral emotional states. Our study was also limited by the sample and size. One strength was that an equal number of males and females were recruited within two major age groups (*peri*-adolescent vs. adult), enabling examination of sex and age as biological variables. We examined but did not find sex differences in our participants. For review on this topic, see work by Cooper and Craft (Cooper & Craft, 2018). Our prior report did identify age-related differences in cognitive and behavioral effects (Murray et al., 2022), however these age-related differences did not extend to the measures reported here. Our sample was limited by the fact that no participant was over the age of 34, and participants were not equally distributed in self-reported reported race/ethnicity. Lastly, we note the inherently exploratory nature of our study as a limitation, as we had no prior anticipation for the magnitude or directionality of effects of THC on many of our measures.

Together, our findings indicate that THC reliably induces robust altered states of consciousness with features shared with classical psychedelics, while also enhancing language entropy and self-reported mind-wandering and mindfulness. These observations point to the utility of THC as a tool for examining features of ASC and for informing the neurobiological basis of potentially beneficial and detrimental effects, from insightfulness and mindfulness to psychosis-mimicking effects. We note that these effects are not mutually exclusive, and ASC may differentially enhance and impair aspects of consciousness simultaneously (Bayne & Carter, 2018). Future studies may work to determine the veracity of reported insightfulness and mindfulness across ASC induction modalities.

*CRediT authorship contribution statement*

**Conor H. Murray:** Conceptualization, Project administration, Methodology, Data curation, Formal analysis, Visualization. **Bhargav Srinivasa-Desikan:** Methodology, Data curation, Formal analysis, Software, Visualization.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon request.

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## Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.concog.2022.103357.

## References

Adam, K. C. S., Doss, M. K., Pabon, E., Vogel, E. K., & de Wit, H. (2020). Δ9-Tetrahydrocannabinol (THC) impairs visual working memory performance: A randomized crossover trial. *Neuropsychopharmacology, 45*(11), 1807–1816. https://doi.org/10.1038/s41386-020-0690-3

Aghajanian, G. K., & Marek, G. J. (2000). Serotonin model of schizophrenia: Emerging role of glutamate mechanisms. *Brain Research. Brain Research Reviews, 31*(2–3), 302–312. https://doi.org/10.1016/s0165-0173(99)00046-6

Amarel, M., & Cheek, F. E. (1965). Some effects of LSD-25 on verbal communication. *Journal of Abnormal Psychology, 70*(6), 453–456. https://doi.org/10.1037/h0022773

Araque, A., Castillo, P. E., Manzoni, O. J., & Tonini, R. (2017). Synaptic functions of endocannabinoid signaling in health and disease. *Neuropharmacology, 124*, 13–24. https://doi.org/10.1016/j.neuropharm.2017.06.017

Baggott, M. J., Kirkpatrick, M. G., Bedi, G., & de Wit, H. (2015). Intimate insight: MDMA changes how people talk about significant others. *Journal of Psychopharmacology, 29*(6), 669–677. https://doi.org/10.1177/0269881115581962

Barrett, F. S., Schlienz, N. J., Lembeck, N., Waqas, M., & Vandrey, R. (2018). "Hallucinations" Following Acute Cannabis Dosing: A Case Report and Comparison to Other Hallucinogenic Drugs. *Cannabis and Cannabinoid Research, 3*(1), 85–93. https://doi.org/10.1089/can.2017.0052

Bartossek, M. T., Kemmerer, J., & Schmidt, T. T. (2021). Altered states phenomena induced by visual flicker light stimulation. *PLoS ONE, 16*(7), e0253779. https://doi.org/10.1371/journal.pone.0253779

Bayne, T., & Carter, O. (2018). Dimensions of consciousness and the psychedelic state. *Neurosci Conscious, 2018*(1), niy008. https://doi.org/10.1093/nc/niy008

Bedi, G., Carrillo, F., Cecchi, G. A., Slezak, D. F., Sigman, M., Mota, N. B., Ribeiro, S., Javitt, D. C., Copelli, M., & Corcoran, C. M. (2015). Automated analysis of free speech predicts psychosis onset in high-risk youths. *npj Schizophrenia, 1*, 15030. https://doi.org/10.1038/npjschz.2015.30

Bedi, G., Cecchi, G. A., Slezak, D. F., Carrillo, F., Sigman, M., & de Wit, H. (2014). A window into the intoxicated mind? Speech as an index of psychoactive drug effects. *Neuropsychopharmacology, 39*(10), 2340–2348. https://doi.org/10.1038/npp.2014.80

Beique, J. C., Imad, M., Mladenovic, L., Gingrich, J. A., & Andrade, R. (2007). Mechanism of the 5-hydroxytryptamine 2A receptor-mediated facilitation of synaptic activity in prefrontal cortex. *Proceedings of the National Academy of Sciences of the United States of America, 104*(23), 9870–9875. https://doi.org/10.1073/pnas.0700436104

Bergen, B. K. (2012). *Louder than words: The new science of how the mind makes meaning*. Basic Books (AZ).

Blei, D. M., & Lafferty, J. D. (2009). Topic models. In *Text mining* (pp. 101–124). Chapman and Hall/CRC.

Blei, D. M., Ng, A. Y., & Jordan, M. I. (2003). Latent dirichlet allocation. *The Journal of Machine Learning Research, 3*, 993–1022.

Bloomfield, M. A. P., Hindocha, C., Green, S. F., Wall, M. B., Lees, R., Petrilli, K., Costello, H., Ogunbiyi, M. O., Bossong, M. G., & Freeman, T. P. (2019). The neuropsychopharmacology of cannabis: A review of human imaging studies. *Pharmacology & Therapeutics, 195*, 132–161. https://doi.org/10.1016/j.pharmthera.2018.10.006

Bossong, M. G., Jansma, J. M., van Hell, H. H., Jager, G., Kahn, R. S., & Ramsey, N. F. (2013). Default mode network in the effects of Δ9-Tetrahydrocannabinol (THC) on human executive function. *PLoS One, 8*(7). https://doi.org/10.1371/journal.pone.0070074. e70074–e70074.

Brewer, J. A., Worhunsky, P. D., Gray, J. R., Tang, Y. Y., Weber, J., & Kober, H. (2011). Meditation experience is associated with differences in default mode network activity and connectivity. *Proceedings of the National Academy of Sciences of the United States of America, 108*(50), 20254–20259. https://doi.org/10.1073/pnas.1112029108

Broyd, S. J., van Hell, H. H., Beale, C., Yucel, M., & Solowij, N. (2016). Acute and Chronic Effects of Cannabinoids on Human Cognition-A Systematic Review. *Biological Psychiatry, 79*(7), 557–567. https://doi.org/10.1016/j.biopsych.2015.12.002

Carbonaro, T. M., Johnson, M. W., Hurwitz, E., & Griffiths, R. R. (2018). Double-blind comparison of the two hallucinogens psilocybin and dextromethorphan: Similarities and differences in subjective experiences. *Psychopharmacology (Berl), 235*(2), 521–534. https://doi.org/10.1007/s00213-017-4769-4

Carhart-Harris, R. L., Erritzoe, D., Williams, T., Stone, J. M., Reed, L. J., Colasanti, A., Tyacke, R. J., Leech, R., Malizia, A. L., Murphy, K., Hobden, P., Evans, J., Feilding, A., Wise, R. G., & Nutt, D. J. (2012). Neural correlates of the psychedelic state as determined by fMRI studies with psilocybin. *Proceedings of the National Academy of Sciences of the United States of America, 109*(6), 2138–2143. https://doi.org/10.1073/pnas.1119598109

Carhart-Harris, R. L., & Friston, K. J. (2019). REBUS and the Anarchic Brain: Toward a Unified Model of the Brain Action of Psychedelics. *Pharmacological Reviews, 71*(3), 316–344. https://doi.org/10.1124/pr.118.017160

Carhart-Harris, R. L., Leech, R., Hellyer, P. J., Shanahan, M., Feilding, A., Tagliazucchi, E., Chialvo, D. R., & Nutt, D. (2014). The entropic brain: A theory of conscious states informed by neuroimaging research with psychedelic drugs. *Frontiers in Human Neuroscience, 8*, 20. https://doi.org/10.3389/fnhum.2014.00020

Carhart-Harris, R. L., Muthukumaraswamy, S., Roseman, L., Kaelen, M., Droog, W., Murphy, K., Tagliazucchi, E., Schenberg, E. E., Nest, T., Orban, C., Leech, R., Williams, L. T., Williams, T. M., Bolstridge, M., Sessa, B., McGonigle, J., Sereno, M. I., Nichols, D., Hellyer, P. J., Hobden, P., Evans, J., Singh, K. D., Wise, R. G., Curran, H. V., Feilding, A., & Nutt, D. J. (2016). Neural correlates of the LSD experience revealed by multimodal neuroimaging. *Proceedings of the National Academy of Sciences of the United States of America, 113*(17), 4853–4858. https://doi.org/10.1073/pnas.1518377113

Cheng, H., Skosnik, P. D., Pruce, B. J., Brumbaugh, M. S., Vollmer, J. M., Fridberg, D. J., O'Donnell, B. F., Hetrick, W. P., & Newman, S. D. (2014). Resting state functional magnetic resonance imaging reveals distinct brain activity in heavy cannabis users - a multi-voxel pattern analysis. *Journal of Psychopharmacology, 28*(11), 1030–1040. https://doi.org/10.1177/0269881114550354

Cohen, T., & Pakhomov, S. (2020). A Tale of Two Perplexities: Sensitivity of Neural Language Models to Lexical Retrieval Deficits in Dementia of the Alzheimer's Type. *arXiv preprint arXiv:2005.03593*.

Cooper, Z. D., & Craft, R. M. (2018). Sex-Dependent Effects of Cannabis and Cannabinoids: A Translational Perspective. *Neuropsychopharmacology, 43*(1), 34–51. https://doi.org/10.1038/npp.2017.140

Corcoran, C. M., Carrillo, F., Fernandez-Slezak, D., Bedi, G., Klim, C., Javitt, D. C., Bearden, C. E., & Cecchi, G. A. (2018). Prediction of psychosis across protocols and risk cohorts using automated language analysis. *World Psychiatry, 17*(1), 67–75. https://doi.org/10.1002/wps.20491

Cortes-Briones, J. A., Cahill, J. D., Skosnik, P. D., Mathalon, D. H., Williams, A., Sewell, R. A., Roach, B. J., Ford, J. M., Ranganathan, M., & D'Souza, D. C. (2015). The psychosis-like effects of Delta(9)-tetrahydrocannabinol are associated with increased cortical noise in healthy humans. *Biological Psychiatry, 78*(11), 805–813. https://doi.org/10.1016/j.biopsych.2015.03.023

Craig, A. D. (2009). How do you feel–now? The anterior insula and human awareness. *Nature Reviews Neuroscience, 10*(1), 59–70. https://doi.org/10.1038/nrn2555

Davis, A. K., Barrett, F. S., May, D. G., Cosimano, M. P., Sepeda, N. D., Johnson, M. W., Finan, P. H., & Griffiths, R. R. (2021). Effects of Psilocybin-Assisted Therapy on Major Depressive Disorder: A Randomized Clinical Trial. *JAMA Psychiatry, 78*(5), 481–489. https://doi.org/10.1001/jamapsychiatry.2020.3285

De Gregorio, D., Aguilar-Valles, A., Preller, K. H., Heifets, B. D., Hibicke, M., Mitchell, J., & Gobbi, G. (2021). Hallucinogens in Mental Health: Preclinical and Clinical Studies on LSD, Psilocybin, MDMA, and Ketamine. *Journal of Neuroscience, 41*(5), 891–900. https://doi.org/10.1523/jneurosci.1659-20.2020

de Souza, L. C., Guimaraes, H. C., Teixeira, A. L., Caramelli, P., Levy, R., Dubois, B., & Volle, E. (2014). Frontal lobe neurology and the creative mind. *Frontiers in Psychology, 5*, 761. https://doi.org/10.3389/fpsyg.2014.00761

Desikan, B. S., Hull, T., Nadler, E. O., Guilbeault, D., Kar, A. A., Chu, M., & Sardo, D. R. L. (2020). comp-syn: Perceptually Grounded Word Embeddings with Color. *arXiv preprint arXiv:2010.04292*.

Devlin, J., Chang, M.-W., Lee, K., & Toutanova, K. (2018). Bert: Pre-training of deep bidirectional transformers for language understanding. *arXiv preprint arXiv:1810.04805*.

Dittrich, A. (1998). The standardized psychometric assessment of altered states of consciousness (ASCs) in humans. *Pharmacopsychiatry, 31*(Suppl 2), 80–84. https://doi.org/10.1055/s-2007-979351

Earleywine, M., Ueno, L. F., Mian, M. N., & Altman, B. R. (2021). Cannabis-induced oceanic boundlessness. *Journal of Psychopharmacology, 35*(7), 841–847. https://doi.org/10.1177/0269881121997099

Elvevag, B., Foltz, P. W., Weinberger, D. R., & Goldberg, T. E. (2007). Quantifying incoherence in speech: An automated methodology and novel application to schizophrenia. *Schizophrenia Research, 93*(1–3), 304–316. https://doi.org/10.1016/j.schres.2007.03.001

Farb, N. A., Segal, Z. V., Mayberg, H., Bean, J., McKeon, D., Fatima, Z., & Anderson, A. K. (2007). Attending to the present: Mindfulness meditation reveals distinct neural modes of self-reference. *Social Cognitive and Affective Neuroscience, 2*(4), 313–322. https://doi.org/10.1093/scan/nsm030

Fortin, D. A., Trettel, J., & Levine, E. S. (2004). Brief trains of action potentials enhance pyramidal neuron excitability via endocannabinoid-mediated suppression of inhibition. *Journal of Neurophysiology, 92*(4), 2105–2112. https://doi.org/10.1152/jn.00351.2004

Gable, S. L., Hopper, E. A., & Schooler, J. W. (2019). When the Muses Strike: Creative Ideas of Physicists and Writers Routinely Occur During Mind Wandering. *Psychological Science, 30*(3), 396–404. https://doi.org/10.1177/0956797618820626

Gevins, A., & Cutillo, B. (1993). Spatiotemporal Dynamics of Component Processes in Human Working-Memory. *Electroencephalography and Clinical Neurophysiology, 87*(3), 128–143. https://doi.org/10.1016/0013-4694(93)90119-G

Gouzoulis-Mayfrank, E., Heekeren, K., Neukirch, A., Stoll, M., Stock, C., Obradovic, M., & Kovar, K. A. (2005). Psychological effects of (S)-ketamine and N, N-dimethyltryptamine (DMT): A double-blind, cross-over study in healthy volunteers. *Pharmacopsychiatry, 38*(6), 301–311. https://doi.org/10.1055/s-2005-916185

Guilbeault, D., Nadler, E. O., Chu, M., Lo Sardo, D. R., Kar, A. A., & Desikan, B. S. (2020). Color associations in abstract semantic domains. *Cognition, 201*. https://doi.org/10.1016/j.cognition.2020.104306

Hadland, K. A., Rushworth, M. F., Gaffan, D., & Passingham, R. E. (2003). The effect of cingulate lesions on social behaviour and emotion. *Neuropsychologia, 41*(8), 919–931. https://doi.org/10.1016/s0028-3932(02)00325-1

Haertzen, C. A., Hill, H. E., & Belleville, R. E. (1963). Development of the Addiction Research Center Inventory (Arci): Selection of Items That Are Sensitive to the Effects of Various Drugs. *Psychopharmacologia, 4*, 155–166. https://doi.org/10.1007/BF02584088

Hartman, R. L., & Huestis, M. A. (2013). Cannabis effects on driving skills. *Clinical Chemistry, 59*(3), 478–492. https://doi.org/10.1373/clinchem.2012.194381

Hase, A., Erdmann, M., Limbach, V., & Hasler, G. (2022). Analysis of recreational psychedelic substance use experiences classified by substance. *Psychopharmacology (Berl), 239*(2), 643–659. https://doi.org/10.1007/s00213-022-06062-3

Huang, Z., Tarnal, V., Vlisides, P. E., Janke, E. L., McKinney, A. M., Picton, P., Mashour, G. A., & Hudetz, A. G. (2021). Anterior insula regulates brain network transitions that gate conscious access. *Cell Rep, 35*(5), 109081. https://doi.org/10.1016/j.celrep.2021.109081

Keeler, M. H., Ewing, J. A., & Rouse, B. A. (1971). Hallucinogenic effects of marijuana as currently used. *American Journal of Psychiatry, 128*(2), 213–216. https://doi.org/10.1176/ajp.128.2.213

Killingsworth, M. A., & Gilbert, D. T. (2010). A wandering mind is an unhappy mind. *Science, 330*(6006), 932. https://doi.org/10.1126/science.1192439

Kiritoshi, T., Ji, G., & Neugebauer, V. (2016). Rescue of Impaired mGluR5-Driven Endocannabinoid Signaling Restores Prefrontal Cortical Output to Inhibit Pain in Arthritic Rats. *Journal of Neuroscience, 36*(3), 837–850. https://doi.org/10.1523/JNEUROSCI.4047-15.2016

Kometer, M., Pokorny, T., Seifritz, E., & Volleinweider, F. X. (2015). Psilocybin-induced spiritual experiences and insightfulness are associated with synchronization of neuronal oscillations. *Psychopharmacology (Berl), 232*(19), 3663–3676. https://doi.org/10.1007/s00213-015-4026-7

Kometer, M., Schmidt, A., Bachmann, R., Studerus, E., Seifritz, E., & Vollenweider, F. X. (2012). Psilocybin biases facial recognition, goal-directed behavior, and mood state toward positive relative to negative emotions through different serotonergic subreceptors. *Biological Psychiatry, 72*(11), 898–906. https://doi.org/10.1016/j.biopsych.2012.04.005

Kovacs, F. E., Knop, T., Urbanski, M. J., Freiman, I., Freiman, T. M., Feuerstein, T. J., Zentner, J., & Szabo, B. (2012). Exogenous and endogenous cannabinoids suppress inhibitory neurotransmission in the human neocortex. *Neuropsychopharmacology, 37*(5), 1104–1114. https://doi.org/10.1038/npp.2011.262

Kuzbiel, D. (2018). Neural correlates of focused attention and open monitoring meditation. *Dissertation*.

Lakoff, G., & Turner, M. (2009). *More than cool reason: A field guide to poetic metaphor*. University of Chicago press.

LaVigne, J. E., Hecksel, R., Keresztes, A., & Streicher, J. M. (2021). Cannabis sativa terpenes are cannabimimetic and selectively enhance cannabinoid activity. *Scientific Reports, 11*(1), 8232. https://doi.org/10.1038/s41598-021-87740-8

Le, Q., & Mikolov, T. (2014). Distributed representations of sentences and documents. International conference on machine learning.

Lebedev, A. V., Kaelen, M., Lovden, M., Nilsson, J., Feilding, A., Nutt, D. J., & Carhart-Harris, R. L. (2016). LSD-induced entropic brain activity predicts subsequent personality change. *Human Brain Mapping, 37*(9), 3203–3213. https://doi.org/10.1002/hbm.23234
Leland, M., John, H., Nathaniel, S., & Lukas, G. (2018). UMAP: Uniform manifold approximation and projection. *Journal of Open Source Software, 3*(29), 861.
Leszczynski, M., Chaieb, L., Reber, T. P., Derner, M., Axmacher, N., & Fell, J. (2017). Mind wandering simultaneously prolongs reactions and promotes creative incubation. *Scientific Reports, 7*(1), 10197. https://doi.org/10.1038/s41598-017-10616-3
Liechti, M. E., Dolder, P. C., & Schmid, Y. (2017). Alterations of consciousness and mystical-type experiences after acute LSD in humans. *Psychopharmacology (Berl), 234*(9–10), 1499–1510. https://doi.org/10.1007/s00213-016-4453-0
Lutz, A., Slagter, H. A., Dunne, J. D., & Davidson, R. J. (2008). Attention regulation and monitoring in meditation. *Trends in Cognitive Sciences, 12*(4), 163–169. https://doi.org/10.1016/j.tics.2008.01.005
Lutz, J., Brühl, A. B., Scheerer, H., Jäncke, L., & Herwig, U. (2016). Neural correlates of mindful self-awareness in mindfulness meditators and meditation-naïve subjects revisited. *Biological Psychology, 119*, 21–30. https://doi.org/10.1016/j.biopsycho.2016.06.010
Mackie, K. (2005). Distribution of Cannabinoid Receptors in the Central and Peripheral Nervous System. In R. G. Pertwee (Ed.), *Cannabinoids* (pp. 299–325). Berlin Heidelberg: Springer. https://doi.org/10.1007/3-540-26573-2_10.
Marggraf, M. P., Cohen, A. S., Davis, B. J., DeCrescenzo, P., Bair, N., & Minor, K. S. (2018). Semantic coherence in psychometric schizotypy: An investigation using Latent Semantic Analysis. *Psychiatry Research, 259*, 63–67. https://doi.org/10.1016/j.psychres.2017.09.078
Martin, W. R., Sloan, J. W., Sapira, J. D., & Jasinski, D. R. (1971). Physiologic, subjective, and behavioral effects of amphetamine, methamphetamine, ephedrine, phenmetrazine, and methylphenidate in man. *Clinical Pharmacology & Therapeutics, 12*(2), 245–258. https://doi.org/10.1002/cpt1971122part1245
Mason, M. F., Norton, M. I., Van Horn, J. D., Wegner, D. M., Grafton, S. T., & Macrae, C. N. (2007). Wandering minds: The default network and stimulus-independent thought. *Science, 315*(5810), 393–395. https://doi.org/10.1126/science.1131295
Miaschi, A., Brunato, D., Dell'Orletta, F., & Venturi, G. (2021). What Makes My Model Perplexed? A Linguistic Investigation on Neural Language Models Perplexity. Proceedings of Deep Learning Inside Out (DeeLIO): The 2nd Workshop on Knowledge Extraction and Integration for Deep Learning Architectures.
Mikolov, T., Sutskever, I., Chen, K., Corrado, G. S., & Dean, J. (2013). Distributed representations of words and phrases and their compositionality. *Advances in Neural Information Processing Systems*.
Miller, E. K., Freedman, D. J., & Wallis, J. D. (2002). The prefrontal cortex: Categories, concepts and cognition. *Philosophical Transactions of the Royal Society of London. Series B, Biological sciences, 357*(1424), 1123–1136. https://doi.org/10.1098/rstb.2002.1099
Milliere, R., Carhart-Harris, R. L., Roseman, L., Trautwein, F. M., & Berkovich-Ohana, A. (2018). Psychedelics, Meditation, and Self-Consciousness. *Frontiers in Psychology, 9*, 1475. https://doi.org/10.3389/fpsyg.2018.01475
Mills, C., Porter, A. R., Andrews-Hanna, J. R., Christoff, K., & Colby, A. (2021). How task-unrelated and freely moving thought relate to affect: Evidence for dissociable patterns in everyday life. *Emotion, No Pagination Specified-No Pagination Specified.*. https://doi.org/10.1037/emo0000849
Morgan, C. J. A., Freeman, T. P., Hindocha, C., Schafer, G., Gardner, C., & Curran, H. V. (2018). Individual and combined effects of acute delta-9-tetrahydrocannabinol and cannabidiol on psychotomimetic symptoms and memory function. *Translational Psychiatry, 8*(1), 181. https://doi.org/10.1038/s41398-018-0191-x
Murray, C. H., Huang, Z., Lee, R., & de Wit, H. (2022). Adolescents are more sensitive than adults to acute behavioral and cognitive effects of THC. *Neuropsychopharmacology*. https://doi.org/10.1038/s41386-022-01281-w
Murray, C. H., Tare, I., Perry, C. M., Malina, M., Lee, R., & de Wit, H. (2021). Low doses of LSD reduce broadband oscillatory power and modulate event-related potentials in healthy adults. *Psychopharmacology (Berl)*. https://doi.org/10.1007/s00213-021-05991-9
Muthukumaraswamy, S. D., Carhart-Harris, R. L., Moran, R. J., Brookes, M. J., Williams, T. M., Errtizoe, D., Sessa, B., Papadopoulos, A., Bolstridge, M., Singh, K. D., Feilding, A., Friston, K. J., & Nutt, D. J. (2013). Broadband cortical desynchronization underlies the human psychedelic state. *Journal of Neuroscience, 33*(38), 15171–15183. https://doi.org/10.1523/JNEUROSCI.2063-13.2013
Nichols, D. E. (2016). Psychedelics. *Pharmacological Reviews, 68*(2), 264–355. https://doi.org/10.1124/pr.115.011478
Nichols, D. E., & Walter, H. (2021). The History of Psychedelics in Psychiatry. *Pharmacopsychiatry, 54*(4), 151–166. https://doi.org/10.1055/a-1310-3990
Nutt, D., Erritzoe, D., & Carhart-Harris, R. (2020). Psychedelic Psychiatry's Brave New World. *Cell, 181*(1), 24–28. https://doi.org/10.1016/j.cell.2020.03.020
Pabon, E., & de Wit, H. (2019). Developing a phone-based measure of impairment after acute oral (9)-tetrahydrocannabinol. *Journal of Psychopharmacology, 33*(9), 1160–1169. https://doi.org/10.1177/0269881119862533
Palhano-Fontes, F., Andrade, K. C., Tofoli, L. F., Santos, A. C., Crippa, J. A., Hallak, J. E., Ribeiro, S., & de Araujo, D. B. (2015). The psychedelic state induced by ayahuasca modulates the activity and connectivity of the default mode network. *PLoS ONE, 10*(2), e0118143. https://doi.org/10.1371/journal.pone.0118143
Perna, D. (1969). Psychotogenic effect of marihuana. *JAMA, 209*(7), 1085–1086. https://www.ncbi.nlm.nih.gov/pubmed/5819660.
Pokorny, T., Preller, K. H., Kometer, M., Dziobek, I., & Vollenweider, F. X. (2017). Effect of Psilocybin on Empathy and Moral Decision-Making. *International Journal of Neuropsychopharmacology, 20*(9), 747–757. https://doi.org/10.1093/ijnp/pyx047
Polito, V., & Stevenson, R. J. (2019). A systematic study of microdosing psychedelics. *PLoS ONE, 14*(2), e0211023. https://doi.org/10.1371/journal.pone.0211023
Preller, K. H., Herdener, M., Pokorny, T., Planzer, A., Kraehenmann, R., Stampfli, P., Liechti, M. E., Seifritz, E., & Vollenweider, F. X. (2017). The Fabric of Meaning and Subjective Effects in LSD-Induced States Depend on Serotonin 2A Receptor Activation. *Current Biology, 27*(3), 451–457. https://doi.org/10.1016/j.cub.2016.12.030
Preller, K. H., Pokorny, T., Hock, A., Kraehenmann, R., Stampfli, P., Seifritz, E., Scheidegger, M., & Vollenweider, F. X. (2016). Effects of serotonin 2A/1A receptor stimulation on social exclusion processing. *Proceedings of the National Academy of Sciences of the United States of America, 113*(18), 5119–5124. https://doi.org/10.1073/pnas.1524187113
Preller, K. H., Razi, A., Zeidman, P., Stampfli, P., Friston, K. J., & Vollenweider, F. X. (2019). Effective connectivity changes in LSD-induced altered states of consciousness in humans. *Proceedings of the National Academy of Sciences of the United States of America, 116*(7), 2743–2748. https://doi.org/10.1073/pnas.1815129116
Radford, A., Wu, J., Child, R., Luan, D., Amodei, D., & Sutskever, I. (2019). Language models are unsupervised multitask learners. *OpenAI blog, 1*(8), 9.
Ruby, F. J., Smallwood, J., Engen, H., & Singer, T. (2013). How self-generated thought shapes mood–the relation between mind-wandering and mood depends on the socio-temporal content of thoughts. *PLoS ONE, 8*(10), e77554. https://doi.org/10.1371/journal.pone.0077554
Sadhasivam, S., Alankar, S., Maturi, R., Vishnubhotla, R. V., Mudigonda, M., Pawale, D., Narayanan, S., Hariri, S., Ram, C., Chang, T., Renschler, J., Eckert, G., & Subramaniam, B. (2020). Inner Engineering Practices and Advanced 4-day Isha Yoga Retreat Are Associated with Cannabimimetic Effects with Increased Endocannabinoids and Short-Term and Sustained Improvement in Mental Health: A Prospective Observational Study of Meditators. *Evidence-Based Complementary and Alternative Medicine, 2020*, 8438272. https://doi.org/10.1155/2020/8438272
Sanz, C., Pallavicini, C., Carrillo, F., Zamberlan, F., Sigman, M., Mota, N., Copelli, M., Ribeiro, S., Nutt, D., & Carhart-Harris, R. (2021). The entropic tongue: Disorganization of natural language under LSD. *Consciousness and Cognition, 87*, 103070.
Schartner, M. M., Carhart-Harris, R. L., Barrett, A. B., Seth, A. K., & Muthukumaraswamy, S. D. (2017). Increased spontaneous MEG signal diversity for psychoactive doses of ketamine, LSD and psilocybin. *Scientific Reports, 7*, 46421. https://doi.org/10.1038/srep46421
Scheibner, H. J., Bogler, C., Gleich, T., Haynes, J. D., & Bermpohl, F. (2017). Internal and external attention and the default mode network. *Neuroimage, 148*, 381–389. https://doi.org/10.1016/j.neuroimage.2017.01.044
Schmidt, T. T., & Berkemeyer, H. (2018). The Altered States Database: Psychometric Data of Altered States of Consciousness. *Frontiers in Psychology, 9*, 1028. https://doi.org/10.3389/fpsyg.2018.01028
Schmidt, T. T., Jagannathan, N., Ljubljanac, M., Xavier, A., & Nierhaus, T. (2020). The multimodal Ganzfeld-induced altered state of consciousness induces decreased thalamo-cortical coupling. *Scientific Reports, 10*(1), 18686. https://doi.org/10.1038/s41598-020-75019-3
Schmidt, T. T., & Prein, J. C. (2019). The Ganzfeld experience-A stably inducible altered state of consciousness: Effects of different auditory homogenizations. *PsyCh Journal, 8*(1), 66–81. https://doi.org/10.1002/pchj.262
Smeekens, B. A., & Kane, M. J. (2016). Working Memory Capacity, Mind Wandering, and Creative Cognition: An Individual-Differences Investigation into the Benefits of Controlled Versus Spontaneous Thought. *Psychol Aesthet Creat Arts, 10*(4), 389–415. https://doi.org/10.1037/aca0000046

Smigielski, L., Kometer, M., Scheidegger, M., Krahenmann, R., Huber, T., & Vollenweider, F. X. (2019). Characterization and prediction of acute and sustained response to psychedelic psilocybin in a mindfulness group retreat. *Scientific Reports, 9*(1), 14914. https://doi.org/10.1038/s41598-019-50612-3

Spencer, T. J., Thompson, B., Oliver, D., Diederen, K., Demjaha, A., Weinstein, S., Morgan, S. E., Day, F., Valmaggia, L., Rutigliano, G., De Micheli, A., Mota, N. B., Fusar-Poli, P., & McGuire, P. (2021). Lower speech connectedness linked to incidence of psychosis in people at clinical high risk. *Schizophrenia Research, 228*, 493–501. https://doi.org/10.1016/j.schres.2020.09.002

Studerus, E., Gamma, A., & Vollenweider, F. X. (2010). Psychometric evaluation of the altered states of consciousness rating scale (OAV). *PLoS ONE, 5*(8), e12412. https://doi.org/10.1371/journal.pone.0012412

Tagliazucchi, E. (2021). Natural Language as a Window into the Subjective Effects and Neurochemistry of Psychedelic Drugs. *Preprints*. https://doi.org/10.20944/preprints202111.0201.v1

Tanay, G., & Bernstein, A. (2013). State Mindfulness Scale (SMS): Development and initial validation. *Psychological Assessment, 25*(4), 1286–1299. https://doi.org/10.1037/a0034044

Tullis, P. (2021). How ecstasy and psilocybin are shaking up psychiatry. *Nature, 589*(7843), 506–509. https://doi.org/10.1038/d41586-021-00187-9

Wachtel, S. R., ElSohly, M. A., Ross, S. A., Ambre, J., & de Wit, H. (2002). Comparison of the subjective effects of Delta(9)-tetrahydrocannabinol and marijuana in humans. *Psychopharmacology (Berl), 161*(4), 331–339. https://doi.org/10.1007/s00213-002-1033-2

Wang, C., Liang, S., Zhang, Y., Li, X., & Gao, T. (2019). Does it make sense? and why? a pilot study for sense making and explanation. *arXiv preprint arXiv:1906.00363*.

Wang, H. T., Poerio, G., Murphy, C., Bzdok, D., Jefferies, E., & Smallwood, J. (2018). Dimensions of Experience: Exploring the Heterogeneity of the Wandering Mind. *Psychological Science, 29*(1), 56–71. https://doi.org/10.1177/0956797617728727

Watts, A. (1968). Psychedelics and religious experience. *California Law Review, 56*, 74.

Xiang, J., Tian, C., Niu, Y., Yan, T., Li, D., Cao, R., Guo, H., Cui, X., Cui, H., Tan, S., & Wang, B. (2019). Abnormal Entropy Modulation of the EEG Signal in Patients With Schizophrenia During the Auditory Paired-Stimulus Paradigm. *Front Neuroinform, 13*, 4. https://doi.org/10.3389/fninf.2019.00004

Yaden, D. B., & Griffiths, R. R. (2021). The Subjective Effects of Psychedelics Are Necessary for Their Enduring Therapeutic Effects. *ACS Pharmacology & Translational Science, 4*(2), 568–572. https://doi.org/10.1021/acsptsci.0c00194

Zaytseva, Y., Horacek, J., Hlinka, J., Fajnerova, I., Androvicova, R., Tintera, J., Salvi, V., Balikova, M., Hlozek, T., Spaniel, F., & Palenicek, T. (2019). Cannabis-induced altered states of consciousness are associated with specific dynamic brain connectivity states. *Journal of Psychopharmacology, 33*(7), 811–821. https://doi.org/10.1177/0269881119849814

Zedelius, C. M., & Schooler, J. W. (2015). Mind wandering "Ahas" versus mindful reasoning: Alternative routes to creative solutions. *Frontiers in Psychology, 6*, 834. https://doi.org/10.3389/fpsyg.2015.00834