Pontifícia Universidade Católica
do Rio de Janeiro

Bheatrix Bienemann Favero

Subjective experiences of classic psychedelic substances users

Tese de Doutorado

Thesis presented to the Programa de Pós-graduação em Psicologia of PUC-Rio in partial fulfillment of the requirements for the degree of Doutor em Psicologia.

Advisor: Prof. Daniel Correa Mograbi

Rio de Janeiro,
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I dedicate this thesis to the more than 650 thousand families who are victims of COVID in Brazil. May science be properly valued in the future so that tragedies like this never happen again.

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Abstract

Bienemann Favero, Bheatrix; Mograbi, Daniel Correa (Advisor). **Subjective experiences of classic psychedelic substances users.** Rio de Janeiro, 2022. 115 p. Tese de Doutorado - Departamento de Psicologia, Pontifícia Universidade Católica do Rio de Janeiro.

Classical psychedelic substances are serotonergic agonists that act essentially on the 5HT2A neurotransmission system. These substances can promote altered states of consciousness, as well as visual, affective, mood, and cognitive changes. Historically, they have been used for ritualistic, recreational, and medicinal purposes. Studies indicate that these substances have low toxicity, low risk of dependence and overdose. There is current scientific interest in the use of these substances as a treatment for a variety of conditions, and while many studies seek to objectively investigate outcomes linked to their use, the subjective contents of the experience of users is seldom explored. Since a first-person perspective is central to the psychedelic experience, this thesis sought to investigate subjective experiences linked to psychedelics through a variety of approaches. First, we sought to adapt and validate the Ego Dissolution Inventory (EDI), an instrument widely used by researchers to assess a central feature of the psychedelic experience, to the Brazilian context (Article 1). Then, we sought to explore public negative (Article 2) and positive (Article 3) reports of psilocybin (the active principle of "magic mushrooms") users, through the Reinert method, which quantitatively analyses transcribed speeches. Finally, the possible influence of altered states of consciousness (ASC), including those linked to use of psychoactive substances, in human evolution was discussed (Article 4), suggesting future research to explore this hypothesis.

Keywords

Psychedelics; Altered States of Consciousness; Ego dissolution; Psilocybin; Magic mushrooms.

Resumo

Bienemann Favero, Bheatrix; Mograbi, Daniel Correa. **Experiências subjetivas de usuários de substâncias psicodélicas clássicas.** Rio de Janeiro, 2022. 115 p. Tese de Doutorado - Departamento de Psicologia, Pontifícia Universidade Católica do Rio de Janeiro.

As substâncias psicodélicas clássicas são agonistas serotoninérgicos que atuam essencialmente no sistema de neurotransmissão 5HT2A. Essas substâncias podem promover estados alterados de consciência, bem como alterações visuais, afetivas, de humor e alterações cognitivas. Historicamente, eles têm sido usados para fins ritualísticos, recreativos e medicinais. Estudos indicam que essas substâncias apresentam baixa toxicidade, baixo risco de dependência e overdose. Existe um interesse científico atual no uso dessas substâncias como tratamento para uma variedade de condições e, embora muitos estudos busquem investigar objetivamente os resultados vinculados ao seu uso, os conteúdos subjetivos da experiência dos usuários ainda são pouco explorados. Considerando que a perspectiva de primeira pessoa é central para a experiência psicodélica, esta tese buscou investigar experiências subjetivas ligadas a psicodélicos por meio de uma variedade de abordagens. Primeiramente, buscou-se adaptar e validar o *Ego Dissolution Inventory* (EDI), instrumento amplamente utilizado por pesquisadores para avaliar um fenômeno essencial da experiência psicodélica, para o contexto brasileiro (Artigo 1). Em seguida, buscou-se explorar relatos públicos negativos (Artigo 2) e positivos (Artigo 3) de usuários de psilocibina (princípio ativo dos "cogumelos mágicos"), por meio do método Reinert, que analisa quantitativamente as falas transcritas. Por fim, discutiu-se a possível influência dos estados alterados de consciência (ASC), incluindo aqueles relacionados ao uso de substâncias psicoativas, na evolução humana (Artigo 4), sugerindo futuras pesquisas para explorar essa hipótese.

Palavras-chave

Psicodélicos; Estados alterados de consciência; Dissolução do ego; Psilocibina; Cogumelos mágicos.

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ARTICLE 1

I. THEORETICAL BACKGROUND

1. Psychedelics

Psychedelics are a class of substances that produce transient but intense changes in perception, mood, and feelings (O'Brien, 2011). These substances act mainly in serotoninergic systems, with compounds that are partial agonists at 5-HT2A serotonin receptors (Ray, 2010). Examples of these compounds are psilocybin (a tryptamine found in certain species of mushrooms), lysergic acid diethylamide (LSD, an ergotamine of fungal origin), mescaline (a phenethylamine from cactus peyote) and N,N-dimethyltryptamine (DMT, a tryptamine of plant origin). Psychedelic substances can produce several effects in perception (e.g. enhanced sensitivity, hallucinations), mood (e.g. elation), emotion (e.g. happiness, anxiety), cognition (e.g. temporal distortions, delusions) and sense of self (e.g. depersonalization, derealisation; Swanson, 2018).

Early studies suggested the therapeutic potentials of these substances, in cases such as supportive care for anxiety in terminal patients (e.g. Kast, 1966; Kurland, 1985), treatment of alcohol and substance addiction (e.g., Chwelos et al., 1959; Smart et al., 1966), and management of personality disorders (Silverman, 1971). After several decades of dormancy (Johnson, Richards, & Griffiths, 2008), interest in research involving the administration of psychedelics to humans was recently restored (Andersen et al., 2021; Bouso et al., 2018; De Gregorio et al., 2020; Galvão-Coelho et al., 2021; Nichols, Johnson, & Nichols, 2017).

The reversible nature of the altered states of consciousness induced by psychedelics, combined with knowledge about these substances generated by traditional use, early and recent scientific studies, makes them a potential tool for experimental investigations of self-awareness. In addition, the use of substances enables both between- and within-group comparisons, for example assessing pre-post differences in the same participants or comparing placebo and intervention groups Finally, the use of psychoactive substances may shed light on the neurochemical underpinnings of self-awareness.

2. Self-awareness and ego-dissolution

The self can be understood as a conceptual constellation (Seth, 2013), referring to a series of components (Lage, Wolmarans, & Mograbi, 2021; Mograbi, Huntley & Critchley, 2021; Northoff & Bermpohl, 2004). Most of our subjective experiences occur from a first-person perspective. William James suggested that feelings and thoughts only exist in relation to an experiencer of the experience (James, 1890/1950), whilst Searle (2007) named this phenomenon first-person ontology. These suggest the notion of a self, an underlying construct that mediates our relationship with the world. Additional evidence for the self comes from alterations in self-experience caused by clinical conditions and use of psychoactive substances, indicating that our experience of the self is shaped by the activity of specific brain regions that underpin this process. Proposing that the self is a process is relevant because it avoids reifying the concept, i.e. suggesting it is a thing inside ourselves, which could lead to an infinite regress (Ryle, 1949).

Psychedelic substances have the capacity of altering the sense of self (Carhart-Harris & Friston, 2010), but few studies have been done in order to understand which specifically functions of self-awareness are modified and at which levels. Recent studies with classic psychedelic substances (e.g., dimethyltryptamine [DMT], psilocybin, LSD) reinforce their potential of altering states of consciousness (Nour & Carhart-Harris, 2017). Changes in the sense of self (e.g. the phenomenon of "ego dissolution") are a fundamental feature in experiences with these substances.

Ego dissolution is a promising topic in the study of human consciousness. It is characterized as the feeling that the self is disintegrating, manifesting as a blurred distinction between subjective and objective perception of the world (Nour, Evans, Nutt, & Carhart-Harris, 2016), also called "ego death" (Johnson, Richards, & Griffiths, 2008, p. 613). This phenomenon can occur commonly in some pathological states, such as in acute psychosis outbreaks or in temporal lobe epilepsy auras; but also in states considered non-pathological, such as in mystical or ritualistic experiences (Nour et al., 2016).

Evidences suggests that psychedelic substances have the ability to rearrange part of the connective network of the brain, altering different functions at the same time

(Lebedev et al., 2015), and this rearrangement is related to changes in self-awareness states (Northoff et al., 2016). This breakdown occurs through silencing old neural connections and establishing new, strong and topologically long-range functional connections that are not usually present in the brain in its unaltered state (Carhart-Harris, Leech, & Tagliazucchi, 2014; Petri et al., 2014; Sampedro et al., 2017). That is, these substances seem to be able to reorganize and increase brain connectivity temporarily, but in a biologically stable way. Regarding psilocybin, for example, the study by Petri et al. (2014) demonstrated increased integration between cortical regions under the influence of the substance – supported by a stable structure of a set of cross-modular connections, probably as a result of stimulation of 5-HT2A receptors in the cortex.

3. Clinical and research implications

Ego dissolution may have important clinical implications, being linked to decreases in depressive symptoms and increased life satisfaction among users (Uthaug et al., 2018). A correlational study found that lifetime use of psychedelic substances in the general population positively predicted nature relatedness and negatively predicted authoritarian political views, in a manner that appears to be mediated by acute and transient "ego dissolution" (Nour et al., 2017). This suggests that ego dissolution is a relevant element involved in the therapeutic action of psychedelics.

Recent studies corroborate previous evidence for psilocybin therapeutic effects (Amsterdam & Brink, 2022; Goldberg et al., 2020; Ross, 2018; Thomas, Malcolm, & Lastra, 2017). The resurgence of research into psychedelics has also included the investigation of substances previously neglected. For example, ayahuasca, an Amazonian Amerindian traditional medicine which has experienced growing use in developed countries (Palamar et al., 2015) has been the target of studies exploring its possible therapeutic effects (e.g., Domínguez-Clavé et al., 2017; Dos Santos et al., 2018; Osório et al., 2015; Palhano-Fontes et al., 2015).

However, although psilocybin has been linked to improved outcomes for conditions such resistant depression, its underlying mechanisms of action, both at neural and psychological levels, remains unclear. It is probable that the beneficial effects of psilocybin are due to changes in self-awareness, particularly in self-focused

processing. This hypothesis finds support not only in previous neuroimaging studies indicating changes in neural networks linked to self-related processing in response to substances with serotoninergic action (e.g., Muthukumaraswamy et al., 2013; Nour et al., 2016; Watts et al., 2017), but also in the phenomenological experience of users describing ego dissolution after consumption of psilocybin (e.g., Letheby & Gerrans, 2017; Roseman, Nutt, & Carhart-Harris, 2018; Nour et al., 2016). It has been suggested that ego dissolution is a process of self-unbinding, i.e., a reduction in self-referential processing (Letheby & Gerrans, 2017). In this sense, ego dissolution may actually represent a deflating of self-focused processing, and this may be the underlying mechanism of improved clinical outcomes after consumption of psilocybin.

II. OBJECTIVES

Based on the theoretical background presented above, this thesis will be composed by four articles: one exploring the psychometric properties of a scale to measure ego dissolution, two observational studies based on negative and positive self-reported experiences with psilocybin and a theoretical article exploring the relationship between the development of complex symbolic thinking and altered states of consciousness in humans. Accordingly, the thesis has the following aims:

- Discuss the phenomenon of ego dissolution and its implications for self-awareness;
- Investigate and compare positive and negative effects resulting from the consumption of psilocybin mushrooms, through public self-reports describing the perception of the users themselves;
- Discuss the hypothesis that consciousness altering states, including psychoactive substances, are associated with the emergence of human symbolic expression in the course of the evolution of our species.

III. ARTICLES SECTION

ARTICLE 1

Bienemann, B., Longo, M. S. C., Etrusco, M. Multedo, M., Cruz, L. V. M., Tófoli, L. F., Mograbi, D. C. Adaptation and latent structure of Brazilian version of the Ego Dissolution Inventory (EDI-BR). (Manuscript submitted for publication).

Abstract

Introduction: Existing scales that seek to measure alterations in self-experience were based on studies conducted in developed countries. Therefore, the aim of this study was to evaluate the psychometric properties of the Ego-Dissolution Inventory (EDI), translate and adapt it to the Brazilian context. **Methods:** Translation of the measure was made by two translators fluent in both English and Portuguese, with back-translation into English to ensure there was no loss of meaning. The scale was included in an online survey exploring substance use. A total of 523 participants answered the full scale. We calculated the Kaiser-Meyer-Olkin (KMO) measure to evaluate sampling adequacy, then ran Exploratory Analysis Factor (EFAs) to investigate the factor structure of the EDI. **Results:** The scale showed excellent internal consistency and sampling adequacy for a factor analysis. Kaiser-Gutman's criteria and Hull's method pointed to a three-factor solution, while Parallel Analysis suggested a two-factor solution. All items showed salient loadings, with two items exhibiting cross-loading. Positive but weak correlations were found between EDI factors 1 and 2 and nature-relatedness. **Conclusions:** The validated scale showed solid psychometric properties, with potential differences in factor structure in relation to the English version. Considering validation as ongoing process, it is recommended to conduct studies comparing the scores of ego dissolution across distinct substances and different regions of the country.

Keywords

Ego-dissolution, ego-death, psychedelics, hallucinogens, psychometrics.

Introduction

Psychedelics are a class of substance that produce transient but intense changes in perception, mood, and feelings.[1] These substances act mainly in serotoninergic systems, through 5-HT_{2A} receptor affinity.[2] Several studies suggest the therapeutic potential of these substances, in cases such as supportive care for anxiety in terminal patients,[3] treatment of refractory depression,[4] and management of substance use disorders.[5]

Ego dissolution (also called "ego death")[6] is a central feature of the psychedelic experience and a promising topic in the study of consciousness. It is characterized as a sensation of blurred distinction between the subjective and objective perception of the world,[7] and feelings of connectedness with the world.[8] This phenomenon can occur in some pathological states, such as in acute psychosis or in temporal lobe epilepsy auras,[9] but also in states considered non-pathological, such as in mystical experiences or through altered states of consciousness induced by hallucinogenic substances.[7]

There are several materials that seek to measure alterations in self-experience. Dittrich's APZ (Abnormal Mental States) questionnaire,[10] as well as its revised versions 5D-ASC and OAV,[11] have been widely used to assess altered states of consciousness caused by psychedelic substances. However, the extensive number of items and the complex 11-factor structure is seen as a limitation by researchers.[7] For this reason, Nour and colleagues sought to develop a measure with a simpler unidimensional structure: the Ego-Dissolution Inventory (EDI).[7] These measures, however, originated from developed countries. To the best of our knowledge, there is no study from developing regions aiming to validate scales measuring ego dissolution. Considering the traditional use of psychedelics in these cultures (e.g. psilocybe mushrooms, ayahuasca, peyote), the absence of adequately validated measures for this population constitutes an important gap in psychedelic science.

Additionally, ego dissolution may have important clinical implications. For example, in a study by Uthaug et al.[12] evaluating long-term effects from ayahuasca use, participants' ego dissolution during psychedelic experiences was strongly linked to decreases in depressive symptoms and increased life satisfaction. This suggests that ego dissolution is a relevant element involved in the therapeutic action

of psychedelics. On the other hand, there is also evidence of negative outcomes – such as bad trips, anxiety, search for emergency medical care – in relation to the phenomenon of ego dissolution.[13] Therefore, it is important that clinical studies with psychedelics seek to measure this construct for a greater understanding of its relationship with positive and negative outcomes. Accordingly, the aim of the current study was to translate and adapt the EDI to the Brazilian context, evaluating its psychometric properties.

Although the final version of the EDI is composed of 8 items referring to the phenomenon of ego dissolution, the original scale included 8 additional items, tapping into the, presumably opposite, phenomenon of ego inflation.[7] Assuming that inflation and dissolution are indeed contrary phenomena, but still in the spectrum of the same construct, we chose to use the original scale of 16 items and evaluate its psychometric structure in a sample from a developing country. It was expected that, as in the original study, the items would group into two different factors: ego dissolution and ego inflation.

Methods

Scale adaptation

Cultural adaptation was done following standard procedures in the field,[14] with translation into Brazilian Portuguese by two translators fluent both in English and Portuguese. Back-translation into English was done by a third translator also fluent in both English and Portuguese, and then compared with the original scale to determine if there were any changes in meaning of items.

The scale was included in an online survey exploring substance use, implemented, and hosted by SurveyMonkey.[15] The full survey took an average of 25 minutes to complete.

Participants

Inclusion criteria for participants were: (1) being at least 18 years old; and (2) having had at least one experience with a classical psychedelic (LSD, psilocybin,

DMT or ayahuasca), MDMA, cocaine, marijuana and/or alcohol. A total of 528 individuals answered the full scale. Sample sociodemographic characteristics can be seen in Table 1.

Table 1 – Sociodemographic characteristics of sample

Variables	n	%
Sex		
Female	312	59.1
Male	210	39.8
Other	6	1.1
Sexual orientation		
Heterosexual	333	63.1
Bisexual	138	26.1
Gay/ Lesbian	45	8.5
Other	12	2.3
Ethnicity/ race (mv = 9)		
White/Caucasian	422	80.0
Afro-descendant	90	17.0
Other	16	3.0
Educational level (mv = 116)		
Elementary school /High School	163	30.9
University education	167	31.7
Graduate education	66	12.5
Other	16	3.0
Marital status		
Single	367	69.5
Married/ Civil union	128	24.2
Divorced/ Widower/ Other	33	6.2
Age*	29.0	9.7

* Mean and standard deviation; mv – missing values

Instruments

In order to explore convergent validity, in addition to the EDI the following instruments were also used:

NR6 – Brief measure of Nature Relatedness Scale[16] (Brazilian version by Longo et al.[17]): This instrument is designed to assess relationship with nature, a construct that

has become increasingly useful in the study of environmental behavior, as well as health and psychological well-being.[16] Recent research indicates that nature relatedness increases after psychedelic use.[18-20] This is a one-dimensional Likert-type six points scale, with higher scores corresponding to higher levels of nature relatedness. The original NR6 version has a Cronbach's alpha (α) mean = .84, with the Brazilian version showing similar internal consistency (α = .86) and factor structure.[17]

SWLS – Satisfaction with Life[21] (Brazilian version by Gouveia et al.[22]): This is a one-dimensional Likert-type scale, with higher scores corresponding to higher levels of satisfaction with life. There is evidence that use of psychedelics increases levels of life satisfaction,[23] and it appears that ego dissolution is significantly related to this specific improvement.[7, 12, 24] The scale has solid psychometric properties (α = .87 for the original scale, α = .81 for Brazilian version).[22]

Statistics

The Kaiser-Meyer-Olkin (KMO) measure was calculated to evaluate sampling adequacy in order to carry out a factor analysis. It has been suggested that KMO values should be equal to or above 0.60 in order to perform and interpret satisfactorily a factor analysis solution.[25] Exploratory Analysis Factor (EFAs) were calculated to investigate the factor structure of the EDI-BR. Principal Axis Factoring was used as the extraction method, with Promax for factor rotation,[26] an oblique method suited for data in which the factors are potentially correlated.[27] Kaiser-Guttman's criteria (*eigenvalue* > 1), Parallel Analysis[28] and Hull's method[29] were used as factor retention methods in three different analyses. Cronbach's alpha was calculated for the full scale, as well as for individual factors. Correlational analyses were calculated between all scale factors and scores in the SWLS and NR6 scales. The analyses were carried out with Factor 10.10.01[30] and IBM SPSS Statistics v.23.[31]

Ethical Issues

This study was approved by a local research ethics committee (CAAE: 95292418.5.0000.8144). All participants provided informed consent before completing the questionnaires.

Results

The KMO index (KMO = .905; Bartlett's test p <. 001) indicated very good sampling adequacy and that the correlation matrix was suitable for factor analysis. Cronbach's alpha was .95 for the full scale.

Exploratory factor analysis

Both Kaiser-Gutman's criteria and Hull's method pointed to a three-factor solution, while Parallel Analysis suggested a two-factor solution. Table 2 shows results for the three-factor solution using Kaiser-Gutman's criteria, while Table 3 displays results for the 2-factor solution.

Table 2 – Factor loadings of the EDI scale items obtained with principal axis factoring analysis and promax rotation

		EDI Factors		
Item #	Item	I	II	III
14	I felt particularly self-confident	**.91**	-.16	.09
16	I felt particularly safe	**.84**	-.05	-.08
8	I felt particularly sure-of-myself	**.81**	-.04	.03
5	I felt a sense of union with others	**.66**	.23	-.12
2	I felt particularly assertive	**.61**	.15	.07
11	I felt far less absorbed by my own issues and concerns	**.51**	.10	.03
10	I felt especially motivated and competitive	**.47**	-.11	.31
9	I experienced a disintegration of my "self" or ego	-.04	**.90**	.05
15	All notion of self and identity dissolved	-.12	**.83**	.08
13	I lost all sense of ego	.02	**.79**	-.02
1	I experienced a dissolution of my "self" or ego	.11	**.78**	-.01
7	I experienced a decrease in my sense of self-importance	-.08	**.58**	.07
3	I felt at one with the universe	**.40**	**.52**	-.13
12	I felt as if my viewpoint was worth more than other peoples’	-.10	.09	**.79**
4	I felt more important or special than others	.02	.11	**.70**
6	My ego felt inflated	.17	-.08	**.65**
Eigenvalue		5.7	2.6	1.4
Variance (%)		35.5	16.2	8.9
Cronbach’s Alpha		.81	.90	.71

Factor loadings greater than 0.4 are represented in bold

Table 3 – Factor loadings of the EDI scale items obtained with parallel analysis and promax rotation

		EDI Factors	
Item #	Item	I	II
1	I experienced a dissolution of my "self" or ego	**.86**	.01
3	I felt at one with the universe	**.68**	.18
5	I felt a sense of union with others	**.45**	**.40**
7	I experienced a decrease in my sense of self-importance	**.63**	-.10
9	I experienced a disintegration of my "self" or ego	**.94**	-.12
13	I lost all sense of ego	**.90**	-.14
15	All notion of self and identity dissolved	**.87**	-.12
2	I felt particularly assertive	.32	**.55**
4	I felt more important or special than others	-.11	**.67**
6	My ego felt inflated	-.24	**.73**
8	I felt particularly sure-of-myself	.16	**.70**
10	I felt especially motivated and competitive	-.11	**.68**
11	I felt far less absorbed by my own issues and concerns	.21	**.43**
12	I felt as if my viewpoint was worth more than other peoples'	-.17	**.65**
14	I felt particularly self-confident	.01	**.83**
16	I felt particularly safe	.14	**.65**
Eigenvalue		6.2	1.8
Variance (%)		45.3	15.1
Cronbach's Alpha		.89	.81

Factor loadings greater than 0.4 are represented in bold

Correlations between EDI factors, NR6 and SWLS

Results can be seen in Table 4. All EDI factors correlated positively moderately. Ego-dissolution did not correlate with SWLS scores. EDI factors 1 and 2 showed weakly positive correlations with NR6 scores.

Table 4 – Correlations between the EDI, NR6 and SWLS

		Factor I	Factor II	Factor III
Spearman's rho	Factor I		.58**	.47**
	Factor II			.35**
	NR6	.22**	.30**	.01
	SWLS	.05	.01	-.07

** p <.01

Discussion

The validated version of the scale showed solid psychometric properties, with excellent internal consistency for the full scale (and excellent to satisfactory consistency for individual factors) and salient loadings for all items. Factor analyses of the EDI-BR indicated different solutions. Analyses based on the Kaiser-Gutman criteria and Hull method pointed to a greater adequacy of the data to a three-factor solution, while parallel analysis suggested a bifactorial solution. All EDI factors correlated positively, and there were weak positive correlations between ego dissolution and nature-relatedness.

In the original validation article,[7] the authors included eight items related to ego dissolution and eight items related to ego inflation. The structure was corroborated by the exploratory factor analysis performed, with retention of factors through parallel analysis. In the present study, although the parallel analysis also pointed to a two-factor solution, items did not behave in the same way. Items specifically referred to the feeling of ego disintegration (e.g. items 1, 3, 5, 7, 9, 13 and 15) gathered in one factor while other items gathered in a second factor. However, in this bifactorial model, item 5 ("I felt union with others") showed cross-loadings (factor 1: .45; factor 2: .40). A possible explanation is that

the item has a generic formulation in relation to who these “others” may be. Alternatively, this may reflect cultural issues (e.g. phenomenon of ego dissolution in Brazil involves a feeling of union with the universe and nature, but not with other people). Another item that deserves attention is #11 (“I felt far less absorbed with my own issues and concerns”), since it surprisingly loaded in the ego-inflation factor. This item also has a formulation that can be problematic as it involves the adverbial intensifier “far less”, which can force more conservative responses. Furthermore, “issues and concerns” are very diverse mental events, which makes the understanding of the item very open to interpretation.

As an alternative to the bifactorial model, a three-factor structure was proposed by the Hull Method and the Kaiser-Gutmann criterion. In this model, items coalesce in aspects related to self-confidence and assertiveness (items 2, 3, 5, 8, 10, 11, 14 and 16), ego dissolution (items 1, 3, 7, 9, 13 and 15) and ego inflation (items 4, 6 and 12). These results indicate a split within ego-inflation items, with some ego-dissolution items also loading on other factors. This means that there may be different possible arrangements between these three domains of the self, in addition to the simple dissolution vs inflation dichotomy. This is represented, for instance, by item 3 (“I felt at one with the universe”), which loaded both in the self-confidence/assertiveness and ego dissolution factors. Perhaps this shows that 'feeling one with the universe' can represent not only ego loss, but also a sense of cognitive empowerment. Further qualitative research may shed light on the specific meaning that users of psychedelics attribute to these concepts.

A three-factor model was also found in the study by Dworatzyk, Jansen & Schmidt[32] that sought to validate the EDI in a German sample. Similarly, the authors found a factorial structure in which the more specific items about ego dissolution also loaded in a factor of their own (except for item 6 "I felt one with the universe" that also carried this factor in our study, but not in the study by Dworatzyk).[32] In addition, the authors found a second factor with six items referring to aspects of ego inflation and a third factor with the items “I felt at one with the universe”, “I felt a sense of union with others”, “I felt far less absorbed by my own issues and concerns” and “I felt particularly sure-of-myself”. The latter two had cross-loadings also with the ego-inflation factor.[32]

In our analyses, factors 1 and 2 of the 3-factor solution were positively correlated with nature-relatedness, even though the correlations were weak. This suggests that the experience of ego dissolution may indeed be conceptualized as bonding with the world, creating higher proximity with nature. Nevertheless, given that the current study is

observational, direction of causality cannot be ascertained, so it is possible that participants with higher nature-relatedness present more intense ego dissolution for other reasons. Also, no factor on the scale showed a statistically significant correlation with the life-satisfaction scale. Given that other studies have demonstrated positive associations between ego dissolution and life satisfaction,[7,23] including a study that used the same measurement scales (EDI and SWLS),[24] it is possible that this reflects cultural issues or sampling biases. Life satisfaction is a construct that greatly varies and is influenced by different factors across cultures.[33, 34] To the best of our knowledge, there is no other data on life satisfaction and psychedelic use in Brazil, so future studies should explore this issue further.

Conclusion

This is the first study to adapt and validate the Ego-Dissolution Inventory in a developing country. Due to the recent explosion of studies with psychedelics, the existence of an instrument duly validated and adapted to evaluate such a central aspect of the psychedelic experience is very relevant. The EDI-BR showed very solid initial psychometric properties and further validation, including establishing the instrument predictive validity, should be pursued. Regarding limitations, some cultural difficulties of translating the term 'ego', as well as the semantic formulation of some items, may have generated conflict in the answers. Additionally, the current study sample was predominantly recruited from college students, which biased its composition towards white ethnicity and higher educational achievement. It is possible that this group is more represented among users of psychedelics. In any case, it would be interesting to conduct new studies with a more diverse sample, perhaps also avoiding biases linked to online data collection. Finally, in order to obtain discriminant validity, it is recommended to conduct studies comparing the scores of ego dissolution across users of different substances. For instance, directly comparing users of substances leading to assertiveness (e.g. methylphenidate), ego-inflation (e.g. cocaine) and ego-dissolution (e.g. psilocybin) would help determining the adequacy of the three-factor solution for the EDI-BR.

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ARTICLE 2

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RESEARCH ARTICLE

Self-reported negative outcomes of psilocybin users: A quantitative textual analysis

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Abstract

Psilocybin, a substance mainly found in mushrooms of the genus psilocybe, has been historically used for ritualistic, recreational and, more recently, medicinal purposes. The scientific literature suggests low toxicity, low risk of addiction, overdose, or other causes of injury commonly caused by substances of abuse, with growing interest in the use of this substance for conditions such as treatment-resistant depression. However, the presence of negative outcomes linked to psilocybin use is not clear yet. The objective of this study is to investigate the negative effects of psilocybin consumption, according to the users' own perception through self-reports extracted from an online platform. 346 reports were analyzed with the assistance of the IRAMUTEQ textual analysis software, adopting the procedures of Descending Hierarchical Classification, Correspondence Factor Analysis and Specificities Analysis. The text segments were grouped in 4 main clusters, describing thinking distortions, emergencies, perceptual alterations and the administration of the substance. Bad trips were more frequent in female users, being associated with thinking distortions. The use of multiple doses of psilocybin in the same session or its combination with other substances was linked to the occurrence of long-term negative outcomes, while the use of mushrooms in single high doses was linked to medical emergencies. These results can be useful for a better understanding of the effects of psilocybin use, guiding harm-reduction initiatives.

Introduction

The growing use of psychedelic substances has been prominent in epidemiological research. According to the United Nations Office on Drugs and Crimes 2019 World Drug Report, there is an upward trend in recent years on quantities of hallucinogenic substances seized all over the world. This is in agreement with reported qualitative information on increasing use of this class of substances recently [1, but see 2]. Data from the 2019 Global Drug Survey indicates that among the 20 drugs used most prominently over the past year, 6 were psychedelic drugs [3]. From 2017 to 2019, "magic mushrooms" (mushrooms from the genus *psilocybe*) in particular had increases in lifetime use from 24.4% to 34.2% and use in the last 12 months from 10.4% to 14.8% [3, 4]. These increases are mirrored by the growth of the new psychoactive substances (NPS) market in Europe in the last years [2], with some NPS attempting to mimic the effects of classic psychedelics.

Psilocybin (4-phosphoryloxy-N,N-dimethyltryptamine), the active ingredient in "magic mushrooms", has been investigated in relation to its medicinal properties, in particular for conditions such as treatment-resistant depression (TRD) [5], with suggestions that psychedelic research may lead to a paradigm shift in psychiatry [6, 7]. Psilocybin has also shown potential clinical benefits for depression and anxiety in end-stage cancer [8], possibly with reductions in death anxiety underpinning its therapeutic effects [9]. Although psilocybin is considered a toxicologically safe substance [10–12], there is no scientific consensus on the risks that the use of psilocybin may bring [13].

In a recent study by Carbonaro et al. [14], 10.7% of users reported that, under psilocybin, they placed themselves or others at risk of physical damage; 2.6% reported being violent or physically aggressive with themselves or others, and 2.7% reported having sought help in a hospital or emergency room. Regarding mental health outcomes, significant associations between the consumption of hallucinogens throughout life and mood, anxiety, personality, eating and substance abuse disorders were found in an epidemiological study [15]. This is in agreement with anecdotal evidence indicating persistent anxiety disorder after consumption of mushrooms containing psilocybin [16].

However, there are divergences relative to these findings. In a populational study by Krebs and Johansen [17], no negative mental health outcomes related to the use of classical psychedelics [LSD (lysergic acid diethylamide), psilocybin, mescaline or peyote

(*Lophophora williamsi*)] were found. In fact, the authors reported findings indicated that the use of psychedelics was associated with decreased mental health problems. Similarly, another large epidemiological study found no relationship between psychedelic use and incidence of psychosis [18]. In addition, some recent studies have demonstrated the potential for psilocybin to treat or alleviate symptoms present in different clinical conditions [e.g. 6,19–21].

The analysis of self-reported user data is a method often neglected in the scientific literature. There are sites exclusively devoted to the storage and dissemination of information about psychoactive substances, with users visiting these sites to informally publish and share reports of their own experiences with different substances and the outcomes they cause. In addition to serving, potentially, to harm reduction purposes, providing access to information for users, these sites create an opportunity for real-time evaluation of emerging drug trends [e.g. 22].

Psilocybin is capable of promoting intense perceptual changes that include hallucinations, synesthesia, and alterations in temporal perception, as well as changes in emotion and thoughts, which may lead to risk of harmful use [23]. In addition, healthy individuals may experience episodes of *bad trips*–negative experiences, which may involve mental confusion, agitation, extreme anxiety, fear and psychotic episodes–including bizarre and frightening images, severe paranoia, and loss of sense of reality [24]. The relationship between *bad trip* episodes and certain mental states and/or physical *settings* is also relevant to consider subjective aspects as important triggers of anxiogenic outcomes related to the use of psychedelic substances. Understanding the specific circumstances in which psilocybin may lead to negative outcomes may have important implications for the future clinical use of this substance, also providing relevant information for harm reduction initiatives.

Considering this, as well as the scarcity of quantitative analyses of self-reported user data, the aim of this work was to investigate negative effects resulting from the consumption of psilocybin, according to the perception of users themselves. Specifically, we sought to investigate the occurrence of health problems caused by the consumption of the substance, negative acute effects and contextual details of the experiences and possible relationships with the negative outcomes.

Methods

Extraction of data and construction of textual corpus

The textual data were obtained from reports manually extracted from the EROWID website (www.erowid.org), a database dedicated to reporting on psychoactive substances and documenting actual reports of users. The reports are reviewed before being published and authors are asked to fulfill certain criteria, such as: description of the context in which the experience was performed and of their previous mental states, details of the preparations made for the use, dosage and time information, observations on possible other medications, herbs or supplements used and a description of the physical and mental effects experienced.

The reports are published anonymously, freely accessible and available on the website in several categories [see 25]. In this research we selected the reports of the subcategories "health problems", "bad trips", "train wreck & trip disasters", present in the category described as Mushrooms (Magic Mushrooms; Psilocybin-containing Fungi). Reports describing the use of mushrooms with substances other than psilocybin as the main active ingredient (e.g. *Amanita muscaria*) were not included. The texts (n = 346) were transcribed manually and any grammar or typing errors were corrected. In addition, some symbols were deleted or replaced (e.g., dashes, quotation marks, indents) to enable analysis by the software. The average length of the reports was 1319.5 words.

In addition, the reports were also categorized according to the following variables: the three subcategories mentioned above ("health problems", "bad trips", "train wreck & trip disasters"), presence of other substances besides mushrooms, dosage, route of administration, form of consumption (dried, tea or fresh and pure) and gender of user (one of the few socio-demographic variables consistently available from the reports). For dosage, a binary variable (doses below and above 5g) was created for the analyses, considering what has been described as a high dose with qualitatively different experiences [26]. Missing values in the variables were classified as *null* and classifications different from the ones mentioned above were classified as *other*. To determine the reliability of the analysis, inter-rater reliability was calculated for all categories that have not been previously provided by the website (i.e., presence of other substances besides mushrooms, dosage, route of administration, form of consumption,

and gender of user; see S1 Fig for a model of report). Total agreement between raters was 92.3%, with a kappa of .85 ($p < .001$).

Data analysis

The participants' answers were initially analyzed qualitatively and freely, in order to generate familiarity with the content. During this stage, the reports were read in detail, one by one, by two members of the research team. Subsequently, the texts were analyzed quantitatively through IRaMuTeQ 0.7 alpha 2 [27] and R 3.1.2. [28]. The analysis was carried out in the textual corpus constructed from the reports and their categorizations, using text segments (TS). TS are divisions of the text, defining the context in which words appear. TS are automatically sized according to the corpus extension; in this study we used the default division provided by Iramuteq (40 words per text segment; please see S1 Fig). We used the procedures of the Descending Hierarchical Analysis (DHA, Reinert Method); Specificities and Correspondence Factor Analysis (CFA). DHA seeks to obtain textual content clusters with specific meanings, resulting from the similarity, association and frequency of their vocabularies. CFA results in a graphical visualization of the proximities, oppositions and tendencies of the text segments (TS) or corpora classes; locating these elements in a Cartesian graph with factors generated from their classifications and allowing graphical visualization of the co-occurrence between words and the possible communities in which they coalesce [29]. Specificities analysis indicates the index of co-occurrence between the words, i.e. the relationship of the words between them and the communities formed by groups composed of the words that are most associated.

The criteria for inclusion of both words and categories in their respective classes by DHA are a frequency greater than the mean of occurrences in the corpus and a chi-square value with the cluster greater than 3.84. The words of interest (active forms) selected for analysis were adjectives, nouns, pronouns, verbs, adverbs and forms not recognized by the IRaMuTeQ dictionary. In addition, when words presented with other associated forms (e.g., test, testing, tested), the most frequent form was chosen for graphic representation. The chi-square test values indicate how strongly words and categories are associated with their clusters [29]. We also reported Cramer's V, a measure of effect size for the association [30]. To avoid inflation of type I error, α was set at .01.

Ethical issues

All materials were anonymized, preventing identification of subjects. Considering that data was public, in agreement with national ethics regulation [31], application for ethics committee approval was dispensed [31; p. 2].

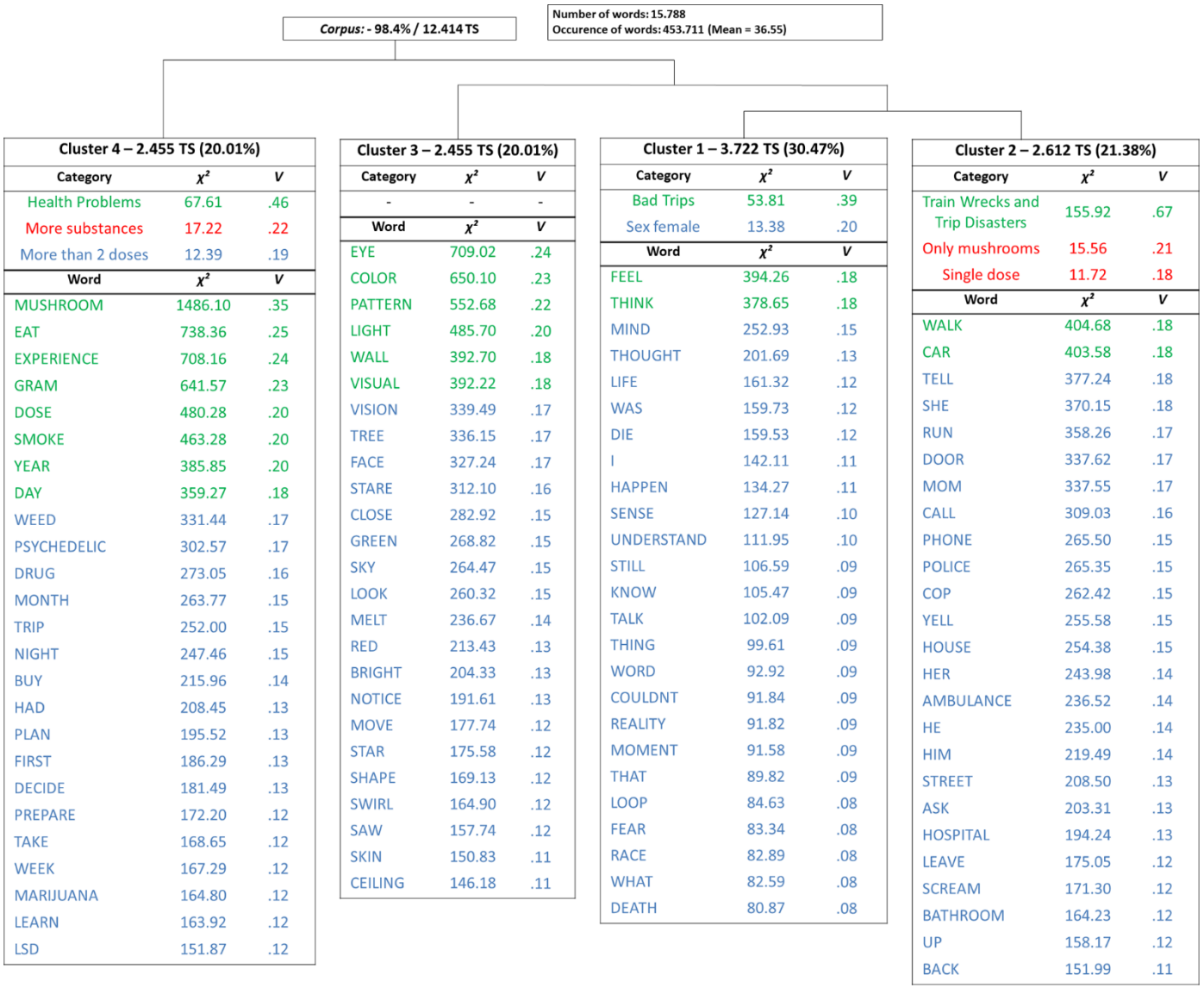
Results

Descending hierarchical analysis

The analysis by DHA retained 98.4% of the total corpus, a percentage indicated as acceptable for the corpus to be considered for this type of analysis [29]. The corpus was divided into 12,215 TS, of which 12,414 (98.4%) were retained, relating 15,788 words that occurred 453,711 times (mean of occurrence for TS = 33.55). Of these, the active forms formed 11,239 words, with 2,637 words with frequency greater than six. As can be seen in dendrogram form (Fig 1), DHA resulted in four clusters of words. Initially, the clusters were grouped into two distinct branches, one composed only of cluster 4 (28.1% of total forms classified) and the other composed of another branch with cluster 3 (20.1%) in one of the extremities and a grouping of clusters 1 (30.5%) and 2 (21.4%) in the other. For the association between words and clusters (degrees of freedom = 3), considering that the 25 words with highest association in each cluster are reported, Cramer's V indicated medium and, particularly in Clusters 3 and 4, large effect sizes [30].

Fig 1. Dendogram with the 25 words with highest χ^2 in each cluster.

Small (red), medium (blue) and large (green) effect sizes, according to [30].



Cluster 4 – 2.455 TS (20.01%)

Category	χ^2	V
Health Problems	67.61	.46
More substances	17.22	.22
More than 2 doses	12.39	.19
Word	**χ^2**	**V**
MUSHROOM	1486.10	.35
EAT	738.36	.25
EXPERIENCE	708.16	.24
GRAM	641.57	.23
DOSE	480.28	.20
SMOKE	463.28	.20
YEAR	385.85	.20
DAY	359.27	.18
WEED	331.44	.17
PSYCHEDELIC	302.57	.17
DRUG	273.05	.16
MONTH	263.77	.15
TRIP	252.00	.15
NIGHT	247.46	.15
BUY	215.96	.14
HAD	208.45	.13
PLAN	195.52	.13
FIRST	186.29	.13
DECIDE	181.49	.13
PREPARE	172.20	.12
TAKE	168.65	.12
WEEK	167.29	.12
MARIJUANA	164.80	.12
LEARN	163.92	.12
LSD	151.87	.12

Cluster 3 – 2.455 TS (20.01%)

Category	χ^2	V
-	-	-
Word	**χ^2**	**V**
EYE	709.02	.24
COLOR	650.10	.23
PATTERN	552.68	.22
LIGHT	485.70	.20
WALL	392.70	.18
VISUAL	392.22	.18
VISION	339.49	.17
TREE	336.15	.17
FACE	327.24	.17
STARE	312.10	.16
CLOSE	282.92	.15
GREEN	268.82	.15
SKY	264.47	.15
LOOK	260.32	.15
MELT	236.67	.14
RED	213.43	.13
BRIGHT	204.33	.13
NOTICE	191.61	.13
MOVE	177.74	.12
STAR	175.58	.12
SHAPE	169.13	.12
SWIRL	164.90	.12
SAW	157.74	.12
SKIN	150.83	.11
CEILING	146.18	.11

Cluster 1 – 3.722 TS (30.47%)

Category	χ^2	V
Bad Trips	53.81	.39
Sex female	13.38	.20
Word	**χ^2**	**V**
FEEL	394.26	.18
THINK	378.65	.18
MIND	252.93	.15
THOUGHT	201.69	.13
LIFE	161.32	.12
WAS	159.73	.12
DIE	159.53	.12
I	142.11	.11
HAPPEN	134.27	.11
SENSE	127.14	.10
UNDERSTAND	111.95	.10
STILL	106.59	.09
KNOW	105.47	.09
TALK	102.09	.09
THING	99.61	.09
WORD	92.92	.09
COULDNT	91.84	.09
REALITY	91.82	.09
MOMENT	91.58	.09
THAT	89.82	.09
LOOP	84.63	.08
FEAR	83.34	.08
RACE	82.89	.08
WHAT	82.59	.08
DEATH	80.87	.08

Cluster 2 – 2.612 TS (21.38%)

Category	χ^2	V
Train Wrecks and Trip Disasters	155.92	.67
Only mushrooms	15.56	.21
Single dose	11.72	.18
Word	**χ^2**	**V**
WALK	404.68	.18
CAR	403.58	.18
TELL	377.24	.18
SHE	370.15	.18
RUN	358.26	.17
DOOR	337.62	.17
MOM	337.55	.17
CALL	309.03	.16
PHONE	265.50	.15
POLICE	265.35	.15
COP	262.42	.15
YELL	255.58	.15
HOUSE	254.38	.15
HER	243.98	.14
AMBULANCE	236.52	.14
HE	235.00	.14
HIM	219.49	.14
STREET	208.50	.13
ASK	203.31	.13
HOSPITAL	194.24	.13
LEAVE	175.05	.12
SCREAM	171.30	.12
BATHROOM	164.23	.12
UP	158.17	.12
BACK	151.99	.11

Correspondence factor analysis

The CFA carried out in order to visualize the relation between the clusters indicated that the clusters are divided mainly in three large areas, with cluster 1 and class 2 being strongly related to each other (Fig 2). In relation to the previous categories of the reports and other variables of interest, it is observed that cluster 1 was significantly associated with the subcategory bad trips (χ^2 (2) = 53.81; p < .001, V = .39) and more frequently reported by female users (χ^2 (2) = 13.38; p < .001, V = .20); cluster 2 with train wrecks and trip disasters (χ^2 (2) = 155.92; p < .001, V = .67), use of just mushrooms (χ^2 (1) = 15.56; p < .001, V = .21) and single doses (χ^2 (4) = 11.72; p < .001, V = .18) and cluster 4 with health problems (χ^2 (2) = 67.61; p < .001, V = .46), multiple doses in the same session (χ^2 (3) = 12.39; p < .001, V = .19) and consumption of other substances besides mushrooms (χ^2 (1) = 17.22; p < .001, V = .22). Cluster 3 did not relate to any category and there were no other significant associations (Fig 3).

Fig 2. Relationship between clusters and words in each cluster.

Red–Cluster 1; green–Cluster 2; blue–Cluster 3; purple–Cluster 4.

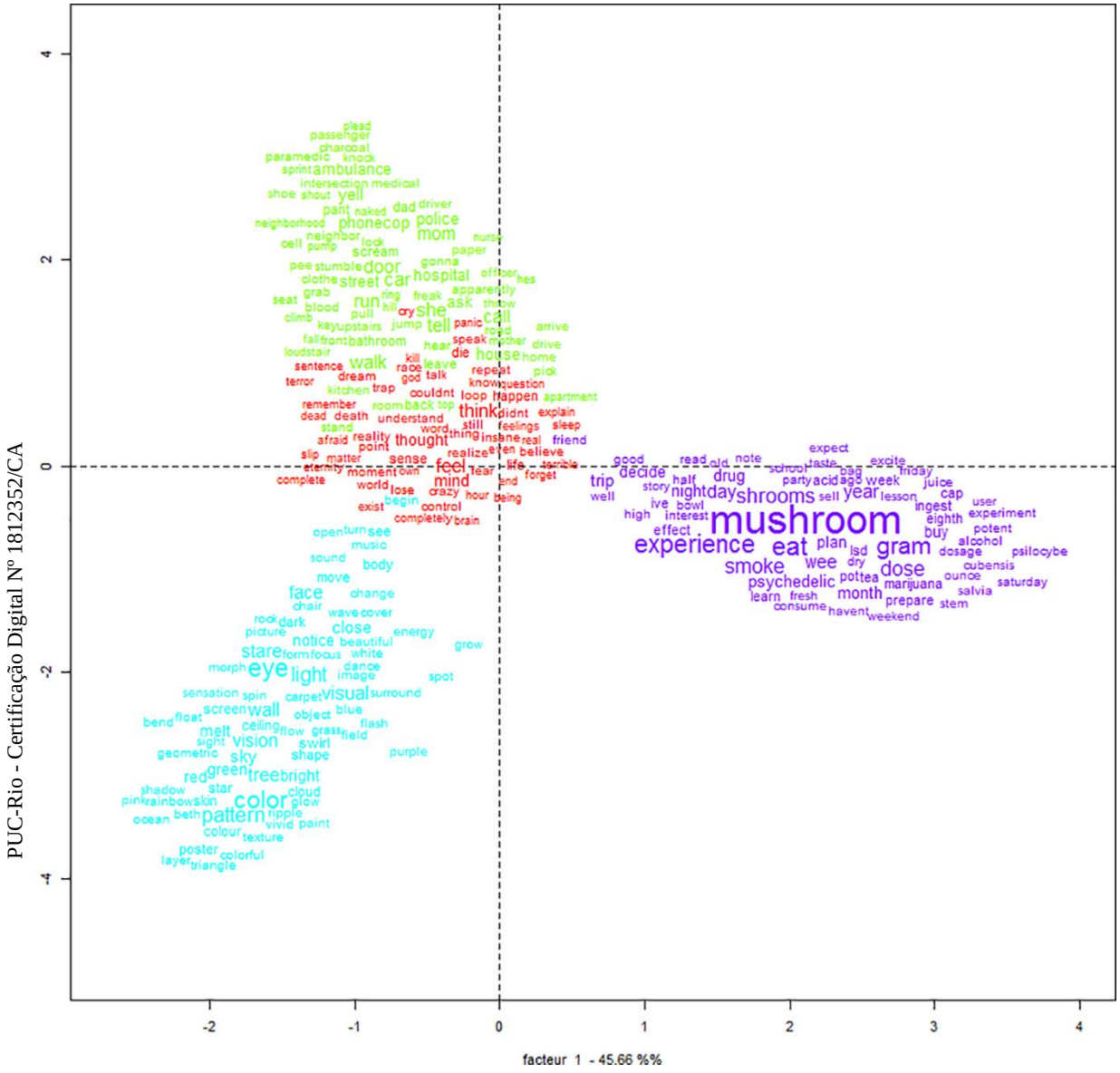
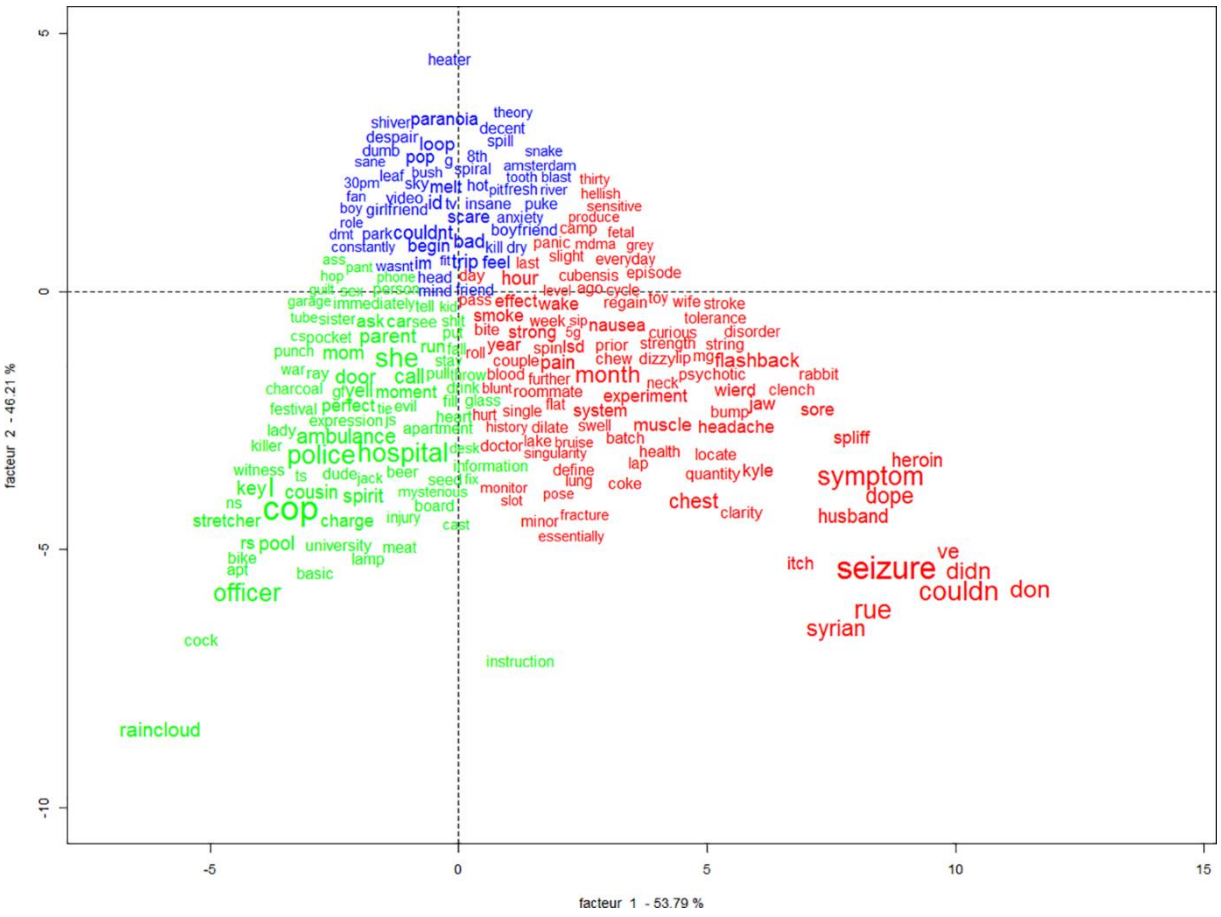


Fig 3. Words relation by cluster and category associated with each cluster.

Words in blue belong to Cluster 1 that relates to category 3 (Bad Trips), words in green to Cluster 2 that relates to category 2 (Train Wrecks and Trip Disasters), words in red belong to Cluster 4 that relates to category 1 (Health Problems). Cluster 3 did not relate to any category and is not represented in the graph.



Specificities analysis

The specificities analysis, indicating the index of co-occurrence between the words, can be seen in Fig 4 (cluster1), Fig 5 (cluster2), Fig 6 (cluster 3) and Fig 7 (cluster 4).

Fig 4. Co-occurrence and communities for words in cluster 1

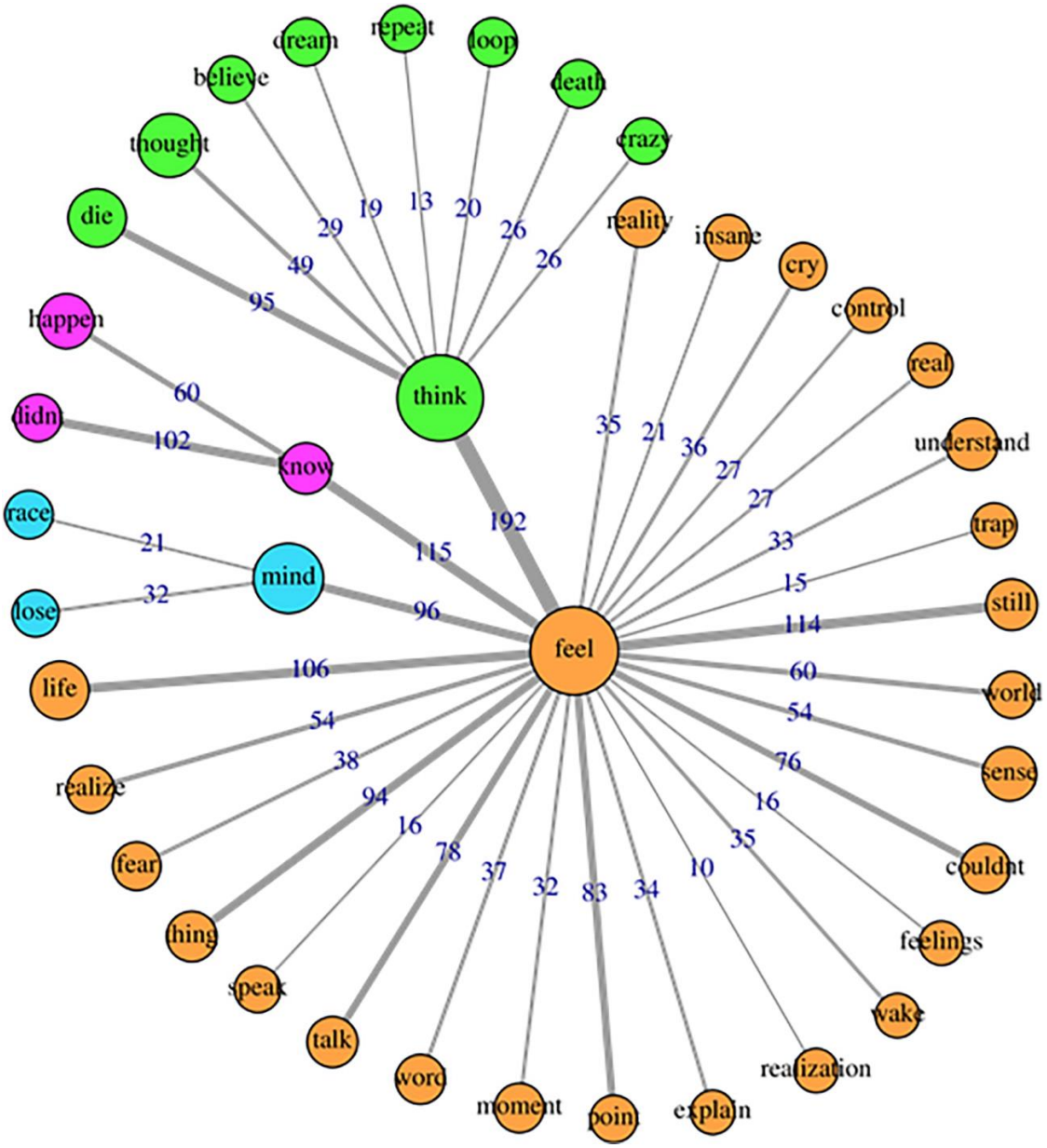


Fig 5. Co-occurrence and communities for words in cluster 2

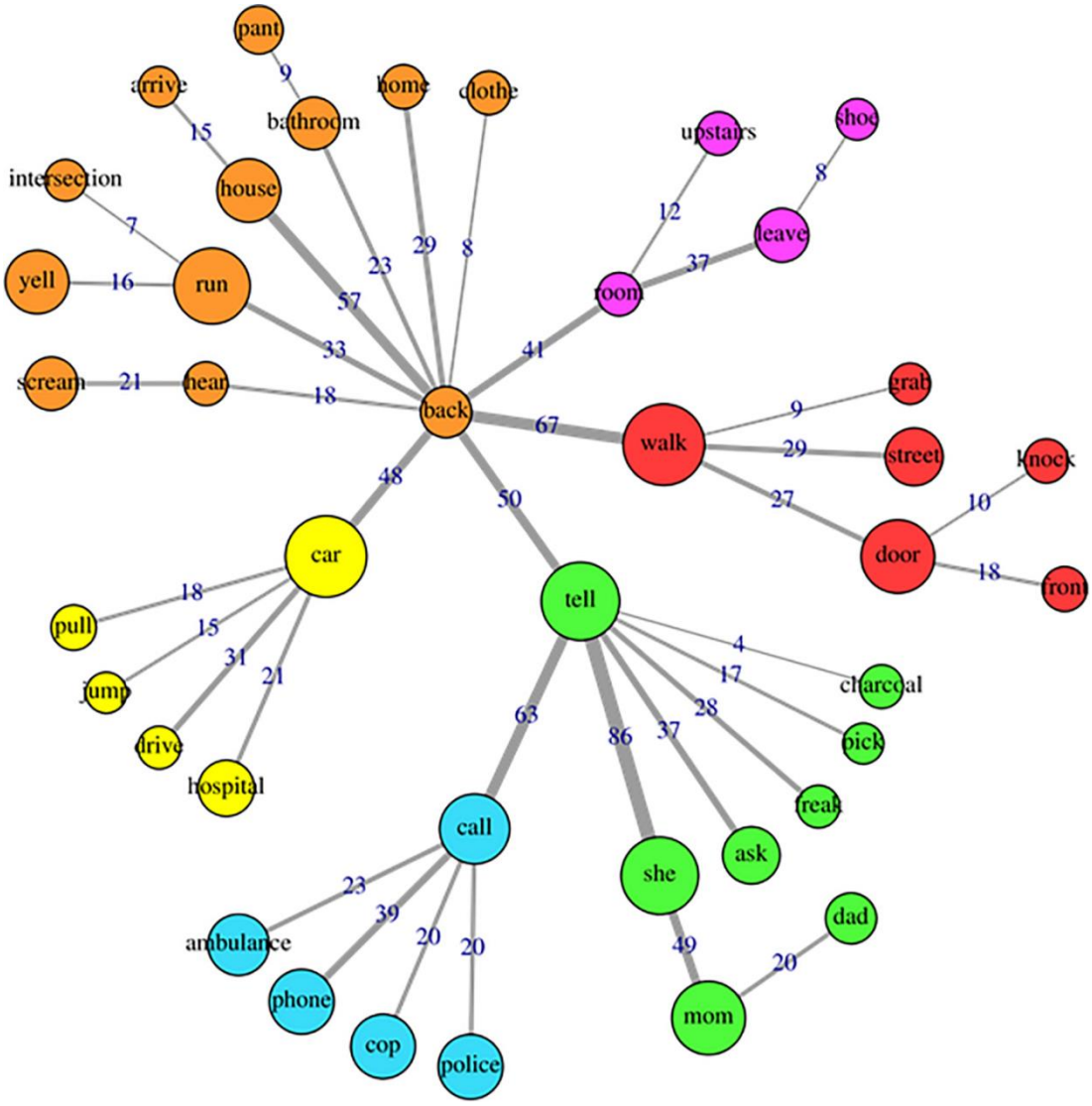


Fig 6. Co-occurrence and communities for words in cluster 3

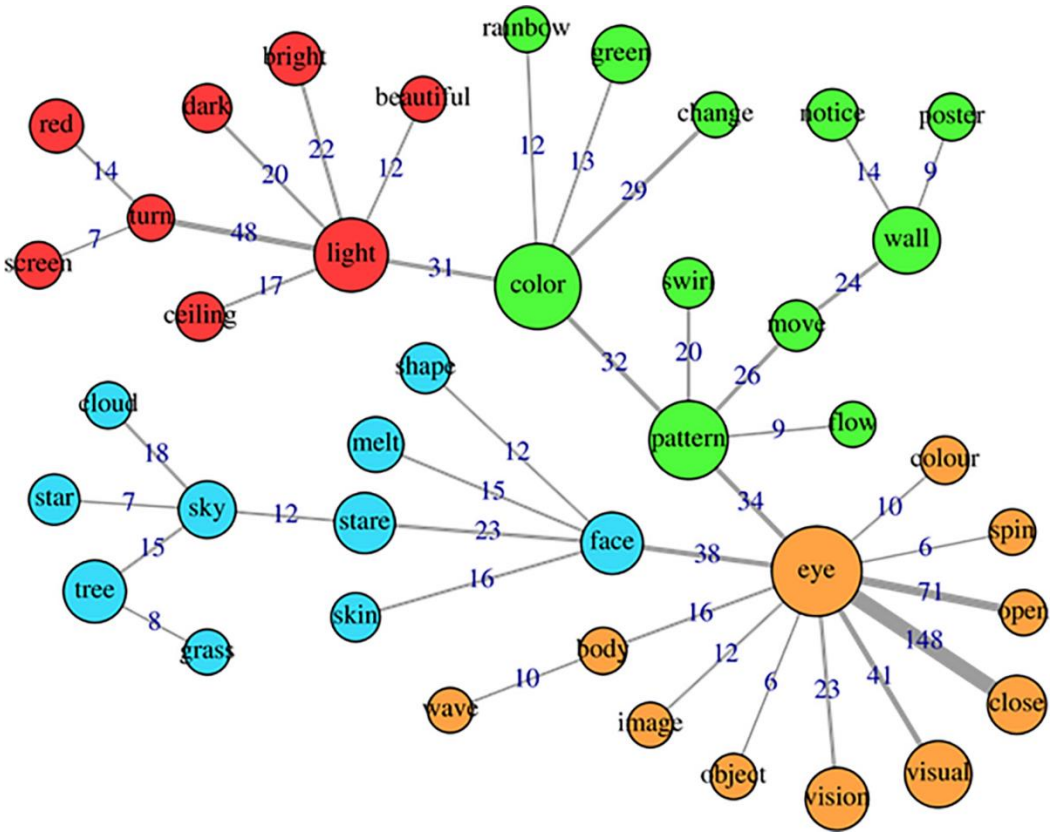
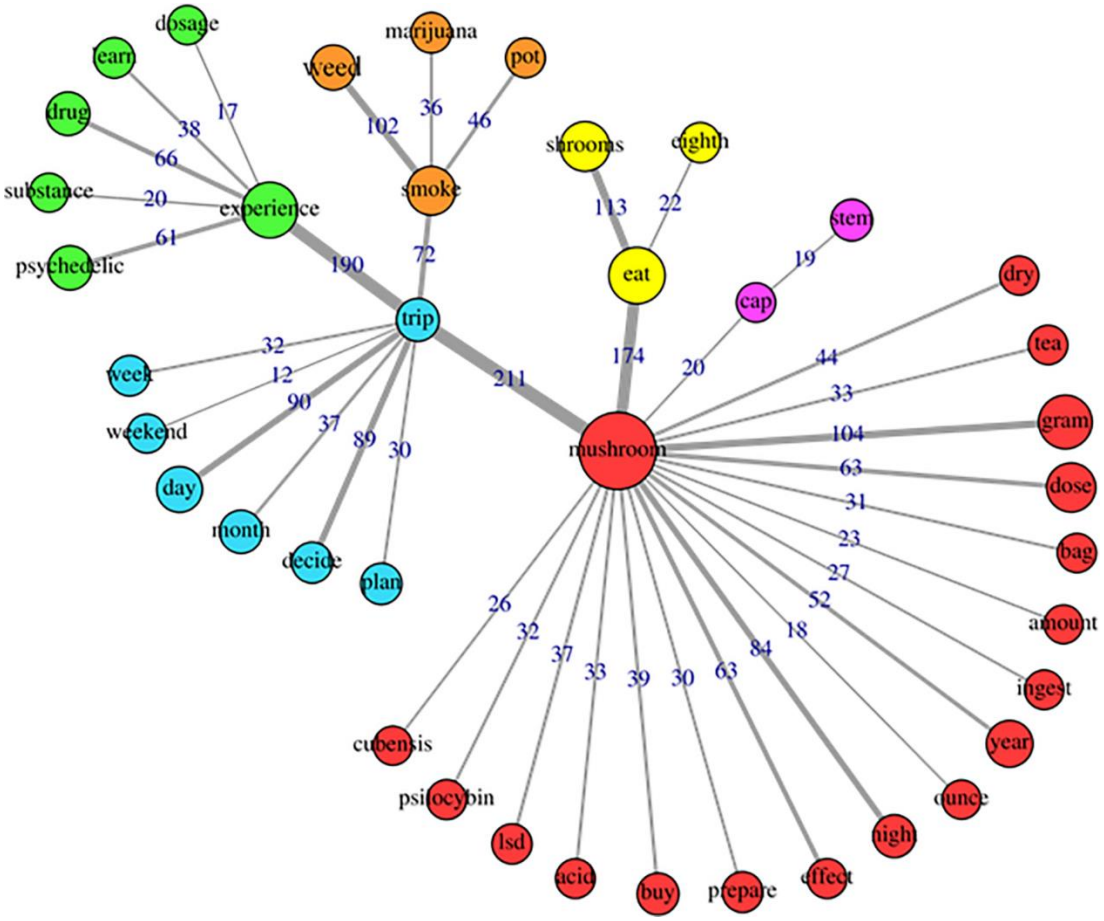


Fig 7. Co-occurrence and communities for words in cluster 4



Discussion

The objective of this study was to analyze reports of experiences with psychedelics that led to negative outcomes, according to the perception of the users themselves. The results indicated that the textual corpus was susceptible to this type of analysis. The textual analysis carried out by means of the DHA gave rise to four clusters of words, i.e. four main fields with different meanings in the participants' reports.

Cluster 1, which included 30.5% of TS, has two main axes: “feel” and “think”. Although the word “feel” may refer to sensorial experiences, the specificities analysis (Fig 4) indicates that these terms were used in reference to mental elucubrations. This is reinforced by the inclusion in the cluster of words and associations such as insane, crazy, mind-race, mind-lose, death, die, fear, among others. The specific contents of this cluster, as well as its association with the category *bad trips*, suggests that short term negative experiences are essentially linked to paranoia and fear/anxiety responses. This is in agreement with previous literature on negative reactions to psychedelics and highlights how these are driven by distortions at the level of thought, co-occurring with anxious states. It suggests that management of anxiety, either by pharmacological or contextual agents (e.g. *setting*) is crucial in the administration of psilocybin. This cluster was also associated with female users. It is possible that this represents stronger effects in women with similar doses of psilocybin, which could be explained by enzymatic, hormonal or social differences between men and women.

Cluster 2, which accounted for 21.4% of TS, has central words linked to action, e.g. walk, back, tell, call, car. Examining the specificities analysis of this class (Fig 5), indicate that the word associations suggest measures that had to be taken in response to the negative experiences. The presence of words such as ambulance, cop, police, hospital and the significant association of this cluster with the train wrecks and trip disasters subcategory indicate the occurrence of emergencies. Such occurrences probably include the need for medical attention, detention by the police force, need for parental help, etc, also requiring transportation, as indicated by words that refer to the process of getting ready, leaving some place, means of transportation, among others.

This cluster was also associated with single doses of psilocybin only. One way to interpret this result is considering a trend for an association between this cluster and doses above 5g ($\chi^2 = 4.22$; $p = .040$), which was not significant considering the established α of .01.

This suggests that emergencies were linked to single high doses of psilocybin, which is relevant in terms of identifying the safety profile of the substance, also establishing a potential benchmark that may increase unwanted consequences accompanying consumption.

It is important to highlight the strong proximity between clusters 1 and 2, as demonstrated by the CFA (Fig 2). The association between both types of experiences suggests that subjective experiences of bad trips are directly linked to emergencies. The direction of causality, however, is not clear. It is possible that emergency procedures were carried out in response to anxiety (e.g. a request for medical care due to excessive fear of dying or going crazy). Conversely, negative emergence outcomes themselves may have contributed further to the occurrence of bad trips, which are often strongly influenced by the setting in which the experience occurred [13,24,32–35], although this is a less straightforward explanation.

Cluster 3 was made up of 20.1% of TS, with words such as eye, color, pattern, light, visual, vision, stare, referring to visual distortions and sensory-perceptual changes in general, which are well known in psychedelic experiments [14,36–38]. The absence of categories significantly associated with this cluster (Fig 1 and Fig 6) is probably explained by the fact that such described effects are common to psychedelics use as a whole, including benign use.

Finally, cluster 4 collected 28.05% of TS, and agglutinated words that seem to refer to the context of psilocybin use (Fig 7), including preparation of mushrooms (e.g. eat, dry, tea), dosage (e.g. dose, gram, bag), use with other substances (e.g. smoke, weed, LSD) and contextual details such as date (e.g. weekend, month). This cluster was associated with the concurrent use of other substances and use of multiple doses in the same session. In addition, this cluster was also associated with the subcategory “health problems”, typically indicative of longer-term complications. It is possible that these complications are consequences of use associated with other substances, given the presence of words like weed, pot, marijuana, LSD, acid. This fact may reinforce the findings about negative outcomes that occur more frequently due to the use of psilocybin associated with other substances, especially alcohol [13,39], and may explain discrepancies in the literature in relation to the association between psychedelic use and negative mental health outcomes.

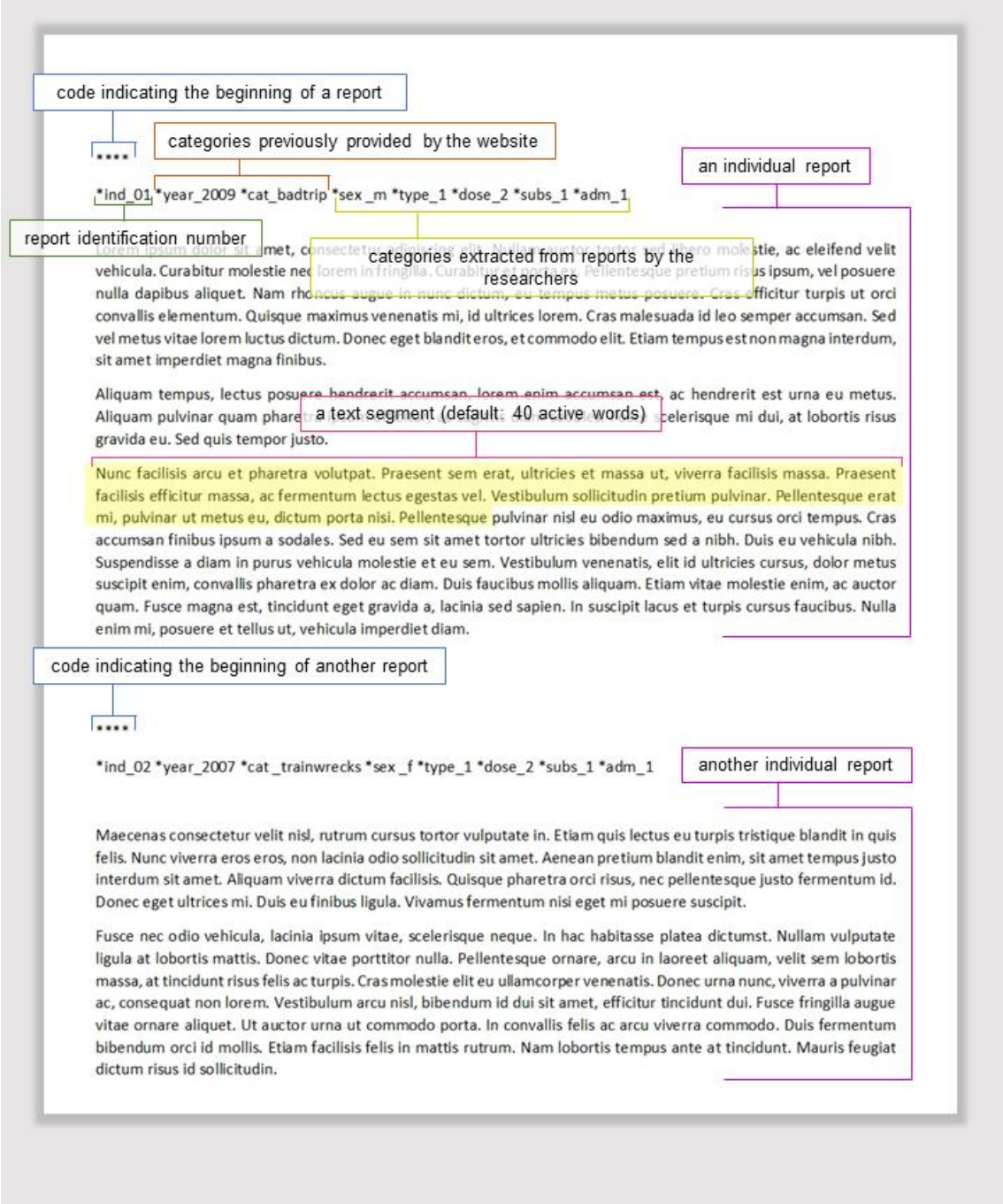
Conclusion

This study aimed to analyze self-reports of negative experiences with psilocybin according to the perception of the users themselves. Psilocybin has been used for centuries, with increased medical interest in recent decades, but the wealth of experience of users has rarely been investigated with sound methodology in the scientific literature. To the best of our knowledge, this is the first study to analyze, using appropriate software, the structure and associations of user self-reported experiences. Findings reinforce the need to manage anxiety during psilocybin administration [24], indicating that distortions at the level of thought were the main cause for bad trips. Additionally, these bad trips were also associated with high doses of psilocybin as well as with emergencies. Longer-term health problems were associated with multiple doses and concurrent use with other substances, in agreement with existing literature [13, 39]. These findings clarify individual and contextual elements that may precipitate negative outcomes linked to psilocybin use, assisting in the elaboration of safety guidelines for users and/or researchers.

The study has a number of important limitations, including a large number of missing values, which prevented the analysis of contextual variables, including setting-specific information. Another limitation refers to sampling, with these reports potentially not representing fully psilocybin users and even with the effective use of substances not being secured in fact, as they only come from reports shared online. This consideration should be done together with the issue of self-selection, that can promote a biased sample with non-probability sampling, considering only experiences that are reported by the users at the website. Additionally, the illegal status of psilocybin is also a potential confounder for results, as the negative outcomes may be connected to black market influences (e.g. different substance being consumed, lack of information about freshness of mushrooms) and not to the substance itself. Nevertheless, given that psilocybin remains being consumed illegally, the current findings provide information valuable to understand use under current circumstances. Finally, the study is exploratory in nature. In this sense, the current study may be used to generate hypotheses by other researchers in the field conducting experimental work, helping to clarify the relationship between contextual variables and subjective effects of psychedelic experience, including the content of the "trips" reported by the users. Further studies are needed to establish more consistently the long and short term consequences of psilocybin use.

Supporting information

S1 Fig



Acknowledgments

The authors acknowledge the work done by Erowid.org in providing information about the use of psychoactive substances and promoting increased awareness on this topic.

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ARTICLE 3

Bienemann, B., Barbosa, A. R., Cruz, L. V. M., Multedo, M., Schenberg, E., Negreiros, M. A., Mograbi, D. C. Health benefits and positive acute effects of psilocybin consumption: A quantitative textual analysis of user self-reported data. (Manuscript submitted for publication).

Abstract

Background: Data shows a growth in the use of psychedelics globally in recent years. In addition to recreational and ritualistic use, recent research into psychedelics has brought advances for treating mental disorders like depression and anxiety, among others. Understanding the specific circumstances in which psilocybin leads to positive outcomes may have important implications for its future clinical use, also providing relevant information for harm reduction initiatives. **Aims**: The aim of this work was to investigate positive effects resulting from the consumption of psilocybin through public self-reports extracted from an online platform. We sought to investigate health benefits promoted by the consumption of the substance, positive acute effects and contextual details of these experiences. **Method**: We analysed 846 reports with the assistance of IRAMUTEQ textual analysis software, adopting the procedures of Descending Hierarchical Classification, Correspondence Factor Analysis and Specificities Analysis. **Results:** The texts were grouped in 5 clusters, describing the content of mental experiences, bodily aspects, perceptual alterations and context of administration of the substance. **Conclusions:** Findings of this study reinforce central axes of the psychedelic experience, such as the presence of somatic and visual alterations, connectedness and feeling one with the world, and effects of setting. The beneficial character of so-called mystical experiences that the substance promotes, and the importance of the ego-dissolution phenomenon are also highlighted. These results can be useful for a better understanding of the effects of psilocybin use, guiding benefit optimization strategies.

Keywords: Psilocybin; psychedelics; mystical experiences; health benefits; positive outcomes.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgments

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Tecnológico (CNPQ - Brazil) and Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ - Brazil).

Introduction

Outside clinical settings there has been a growing use of psychedelics in the general population. From 2015 to 2021, "magic mushrooms" (mushrooms that contains psilocybin) had increases in lifetime users from 25% to 33% and from 9% to 16% for use in the last 12 months (Global Drug Survey, GDS, 2022). Additionally, recent decriminalization of psilocybin mushrooms in several cities/states (e.g. Oregon, Seattle, Detroit) will probably increase its documented use. This highlights that addressing the potential impact, both in terms of benefits and harms, of psilocybin is a research priority.

In addition to recreational and ritualistic use, recent research into psychedelics has brought advances for treating mental disorders like depression and anxiety, for which there has been very little pharmacological innovation. Despite great public health need, the beginning of the 21st century was characterised by a paucity of pharmacological innovation in the treatment of mental illnesses (Hyman, 2014). Between 20 and 30% of patients suffering from depression do not respond to treatment, leading to lower quality of life and higher medical costs (Olchanski et al., 2013). Psilocybin has been shown to be effective against treatment resistant depression in randomised placebo controlled studies (Luoma et al., 2020), and in a head-to-head comparison it has shown better but not statistically superior results to escitalopram (Carhart-Harris et al., 2021). Recent meta-analytic approaches have reinforced these results (Yu et al., 2022). Psilocybin has also produced substantial and sustained decreases in anxiety, depression and suicidal ideation in life-threatening cancer patients (Griffiths et al., 2016; Ross et al., 2021).

However, these findings have been discussed critically, with some considerations about the harm potential of magic mushrooms use (Amsterdam, 2011). Healthy individuals may also experience mental confusion, agitation, extreme anxiety, fear and psychotic episodes–including bizarre and frightening images, severe paranoia, and loss of sense of reality (Johnson, 2018). In addition, a recent epidemiological study found significant associations between the consumption of hallucinogens throughout life and some negative outcomes, including suicide attempts (Shalit, 2019).

Despite psilocybin being considered a toxicologically safe substance (Johnson, 2018; Rucker, 2016), individual and contextual elements are crucial to predict whether an experience will be perceived as positive and produce therapeutic effects. Therefore, despite the growing number of clinical studies with psilocybin, it is also important to investigate effects in uncontrolled real-life event settings. In a previous study, we found evidence of negative outcomes such as bad trips, anxiety, search for emergency medical care and health problems (Bienemann et al., 2020) using self-reports extracted from an online platform.

Understanding the specific circumstances in which psilocybin leads to positive outcomes may have important implications for the future clinical use of this substance, also providing relevant information for harm reduction initiatives. Nevertheless, there is still a scarcity of quantitative analyses of self-reported user data, which is frequently neglected in clinical studies. Considering this, the aim of this work was to investigate positive effects resulting from the consumption of psilocybin through public self-reports extracted from an online platform. Specifically, we sought to investigate health benefits promoted by the consumption of the substance, positive acute effects, and contextual details of these experiences.

Methods

Extraction of data and construction of textual corpus

Text data are from reports manually extracted from the EROWID website (www.erowid.org), a database dedicated to reporting effects of psychoactive substances and documenting actual reports from users. Reports are reviewed before publication and authors are asked to meet certain criteria, such as: description of the context in which they had the experience; their previous mental state; details of the preparations made for ingestion; details of dosage and timing; observations of any other medications or substances ingested; and a description of the physical and mental effects experienced. The reports are published anonymously, are freely accessible and available on the website in different categories (Erowid, 1995). For this study, we selected the reports in the subcategories "health benefits", "medical uses", "glowing experiences" and "mystical experiences" included in the category "mushrooms" (magic mushrooms; psilocybin-

containing mushrooms). Reports describing the use of mushrooms with substances other than psilocybin as the main active ingredient (e.g. Amanita muscaria) were not included. The texts (n = 846) were transcribed manually and any grammatical or typing errors were corrected. In addition, some symbols were deleted or replaced (e.g. hyphens, inverted commas, dashes) to allow analysis by the software. The average length of the reports was 36.48 words. In addition, the reports were also categorized according to the following variables: the subcategories mentioned above ("health benefits", "medical uses", "glowing experiences" and "mystical experiences"), presence of substances other than mushrooms, dosage, route of administration and gender of the user. For dosage, a binary variable (doses below and above 5g) was created for the analyses, taking into account what has been described as a high dose with qualitatively different experiences (Oss & Oeric, 1993). Missing values in the variables were classified as null and classifications differing from those above were classified as other (i.e., presence of substances other than mushrooms, dosage, route of administration, form of consumption and sex of the user; see Supplementary Material 1 for a model of the report).

Data analysis

The participants' answers were first evaluated qualitatively and freely to create familiarity with the content. In this phase, the reports were read in detail one after the other by two members of the research team. Subsequently, the texts were analysed quantitatively using IRaMuTeQ 0.7 alpha 2 (Ratinaud & Marchand, 2012) and R 3.1.2. (R Core Team, 2017). The analysis was conducted in the text corpus created from the reports and their categorisations using text segments (TS). TS are subdivisions of the text that define the context in which words appear. TS are automatically divided according to corpus extension; in this study, we used the standard division provided by Iramuteq (40 words per text segment; see S1 figure). We used the procedures of Descending Hierarchical Analysis (DHA, Reinert method), specificities analysis, and Correspondence Factor Analysis (CFA). DHA aims to obtain content text clusters with specific meanings based on the similarity, association, and frequency of their vocabularies. CFA leads to a graphical visualisation of the proximity, contrasts, and tendencies of text segments (TS) or corpora clusters. It locates these elements in a Cartesian graph with factors generated from their classifications and allows a graphical visualisation of the co-occurrence of words and the possible communities in which they cluster (Loubère & Ratinaud, 2014).

The analysis of specificities shows the index of co-occurrence between words, i.e., the relationship of words to each other and the communities formed by groups consisting of the most strongly associated words.

The criteria for including words and categories in their respective clusters by DHA are a frequency greater than the mean of occurrences in the corpus and a chi-square value with the cluster greater than 3.84. The words of interest (active forms) selected for analysis were adjectives, nouns, pronouns, verbs, adverbs, and forms not recognised by the IRaMuTeQ dictionary. In addition, when words with other associated forms occurred (e.g., test, testing, tested), the most frequent form was selected for graphing. Chi-square test values indicate how strongly words and categories are associated with their clusters (Loubère & Ratinaud, 2014). We also reported Cramer's V, a measure of effect size of association (Kim, 2017). To avoid inflation of type I errors, α was set to .01.

Ethical issues

All materials were anonymized, preventing identification of the subjects. Considering that the data were public, in accordance with national ethics regulations, application for ethics committee approval was dispensed (Ministry of Health, 2016).

Results

Descending hierarchical analysis

The analysis by DHA retained 84.5% of the total corpus, a percentage indicated as acceptable for the corpus to be considered for this type of analysis. The corpus was divided into 37.033 TS, relating 29.093 words that occurred 1.351.032 times (mean of occurrence for TS = 36.5). Of these, the active forms formed 21.181 words, with 2.849 words with frequency equal or greater than 19.

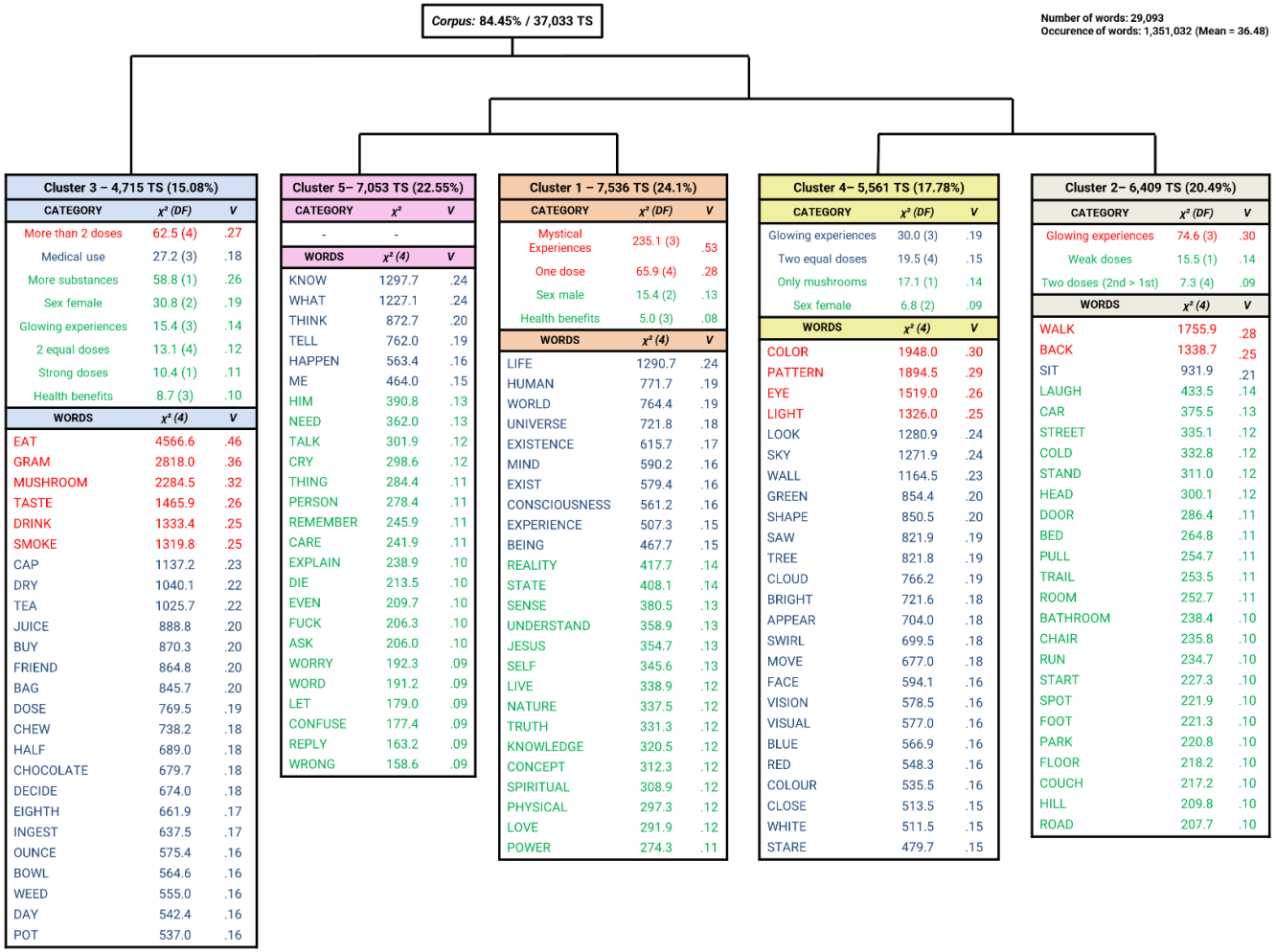
As can be seen in dendrogram form (Figure 1), DHA resulted in five clusters of words. Initially, the clusters were grouped into two distinct branches: one composed only of Cluster 3 (15.08% of total forms classified); and another split into two other branches, combining, respectively, Clusters 5 (22.55%) and 1 (24.1%), and 4 (17.78%) and 2 (20.49%). For the association between words and clusters (degrees of freedom = 4),

considering the 25 words with highest association in each cluster, Cramer's V indicated medium and, particularly in Clusters 2, 3 and 4, large effect sizes.

Figure 1 also shows the association of previous categories of the reports and variables of interest with each cluster. Cluster 1 was significantly associated with the subcategory mystical experiences [χ^2 (3) = 235.1; p < .001; V = .53] and health benefits [χ^2 (3) = 5.0; p = .026; V = .08], one single dose [χ^2 (4) = 65.9; p < .001; V = .28] and more frequently reported by male users [χ^2 (2) = 15.4; p < .001; V = .13]. Cluster 2 was significantly associated with the subcategory glowing experiences [χ^2 (3) = 74.6; p < .001; V = .30], with weak doses [χ^2 (1) = 15.5; p < .001; V = .14] and with a second dose larger than the first [χ^2 (4) = 7.3; p = .007; V = .09]. Cluster 3 was strongly associated with more than two doses [χ^2 (4) = 62.5; p < .001; V = .27], moderately associated with subcategory medical use [χ^2 (3) = 27.2; p < .001; V = .18] and slightly associated with consumption of other substances besides mushrooms [χ^2 (1) = 58.8; p < .001; V = .26], female users [χ^2 (2) = 30.8; p < .001; V = .19], glowing experiences [χ^2 (3) = 15.4; p < .001; V = .14], two equal doses [χ^2 (4) = 13.1; p < .001; V = .12], strong doses [χ^2 (1) 10.4; p = .001; V = .11] and health benefits [χ^2 (3) = 8.7; p = .003; V = .10]. Cluster 4 was moderately associated with the subcategory glowing experiences [χ^2 (3) = 30.0; p < .001; V = .19], with two equal doses [χ^2 (4) = 19.5; p < .001; V = .15], and slightly associated with use of just mushrooms [χ^2 (1) = 17.1; p < .001; V = .14] and female users [χ^2 (2) = 6.8; p = .009; V = .09]. Cluster 5 did not show significant associations with any category.

Figure 1 – **Dendogram with the 25 words with highest χ2 in each cluster**

Large (red), medium (blue) and small (green) effect sizes, according to Kim (2017).

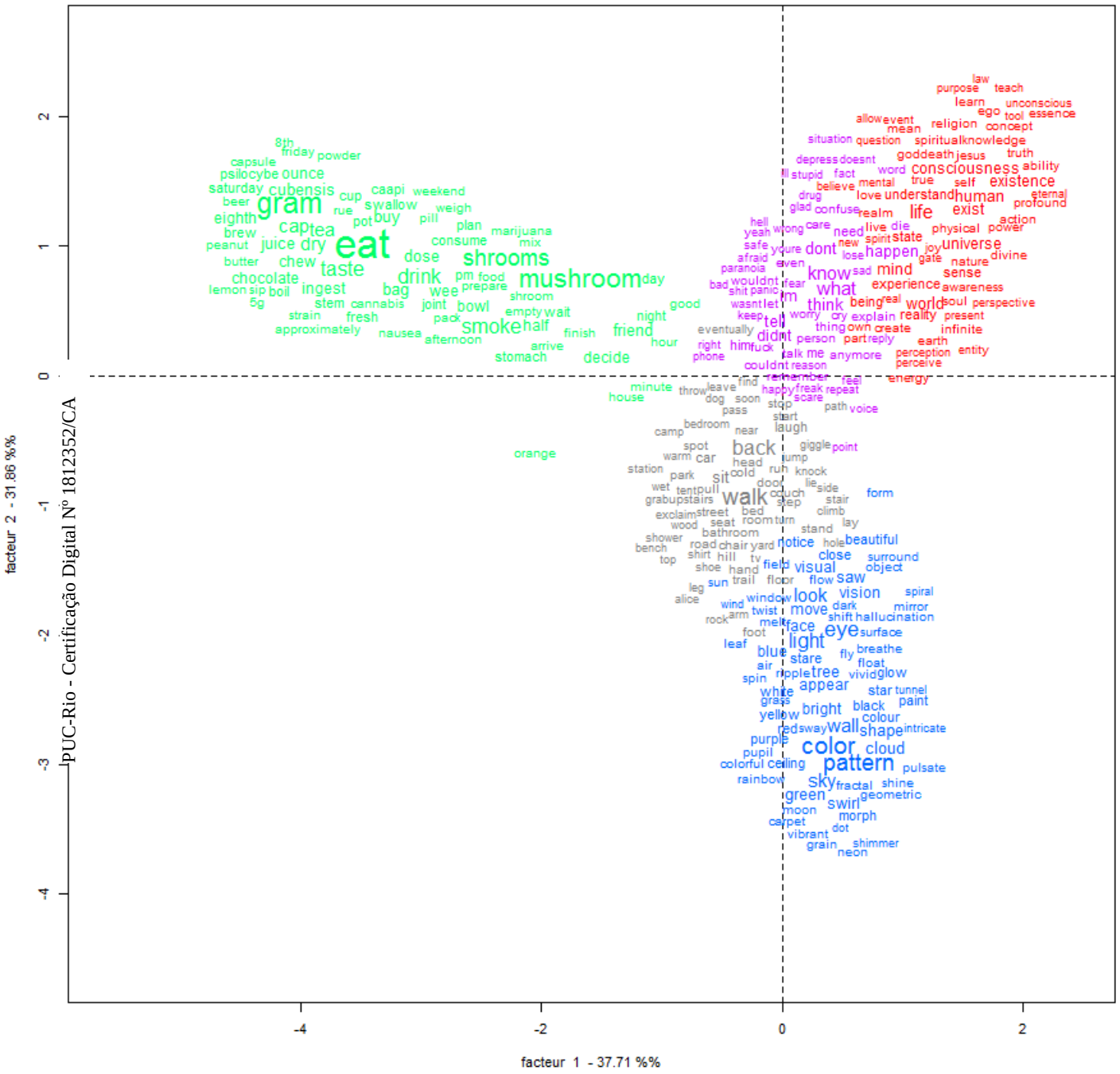


Correspondence factor analysis

The CFA carried out in order to visualize the relation between the clusters indicated that the clusters are divided mainly in three areas, with cluster 1 (red) and 5 (pink) being strongly related to each other. Cluster 2 (gray) and 4 (blue) are slightly related (Figure 2). We can see that Cluster 3 is isolated than another ones, located on the other side of chart.

Figure 2 – **Relationship between clusters and words in each cluster.**

Red–Cluster 1; gray–Cluster 2; green–Cluster 3; blue–Cluster 4; pink–Cluster 5



Specificities analysis

The specificities analysis, indicating the index of co-occurrence between the words, can be seen in Figures 3 (cluster1), 4 (cluster2), 5 (cluster 3), 6 (cluster 4) and 7 (cluster 5).

Figure 3 – **Co-occurrence and communities for words in cluster 1**.

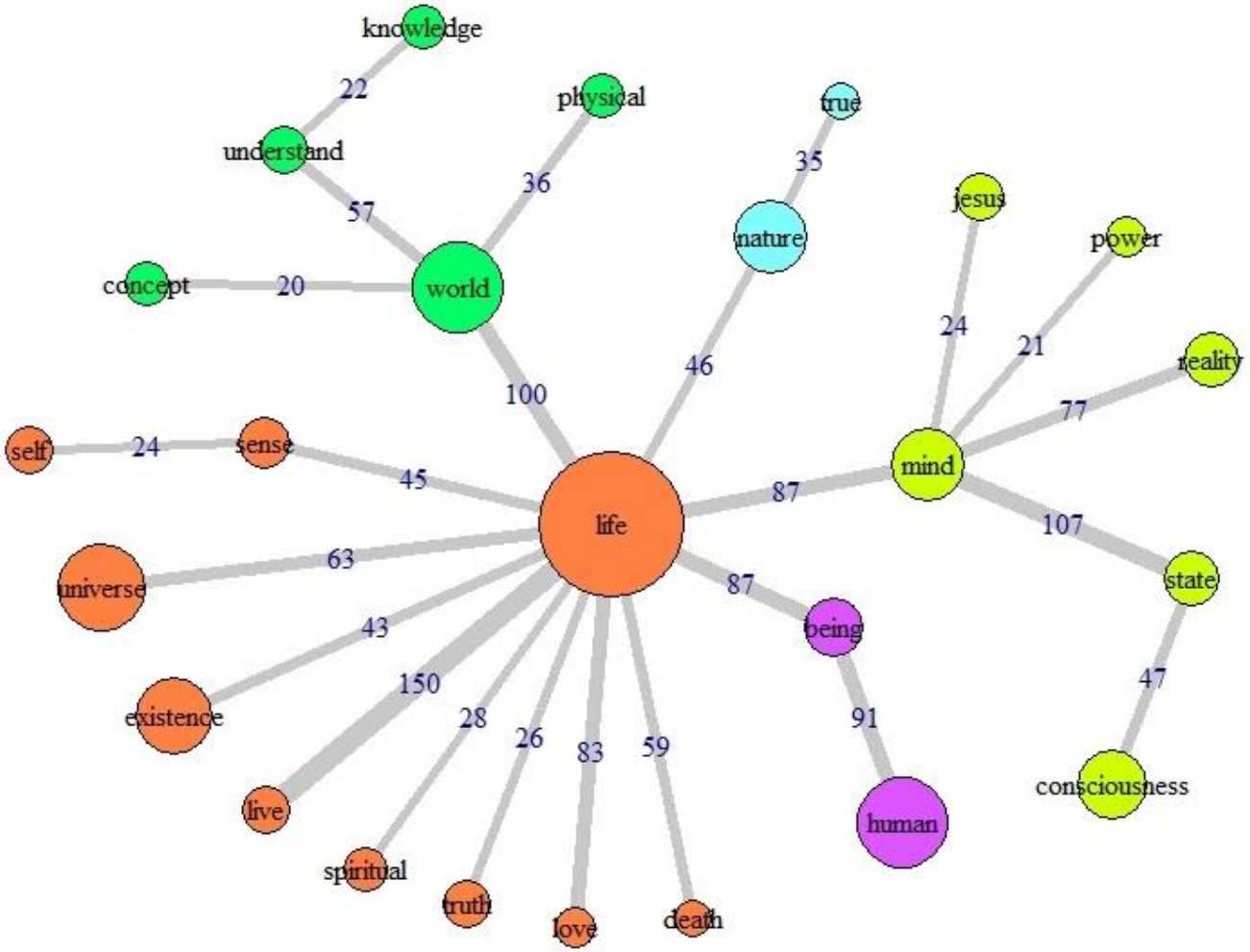


Figure 4 - **Co-occurrence and communities for words in cluster 2**

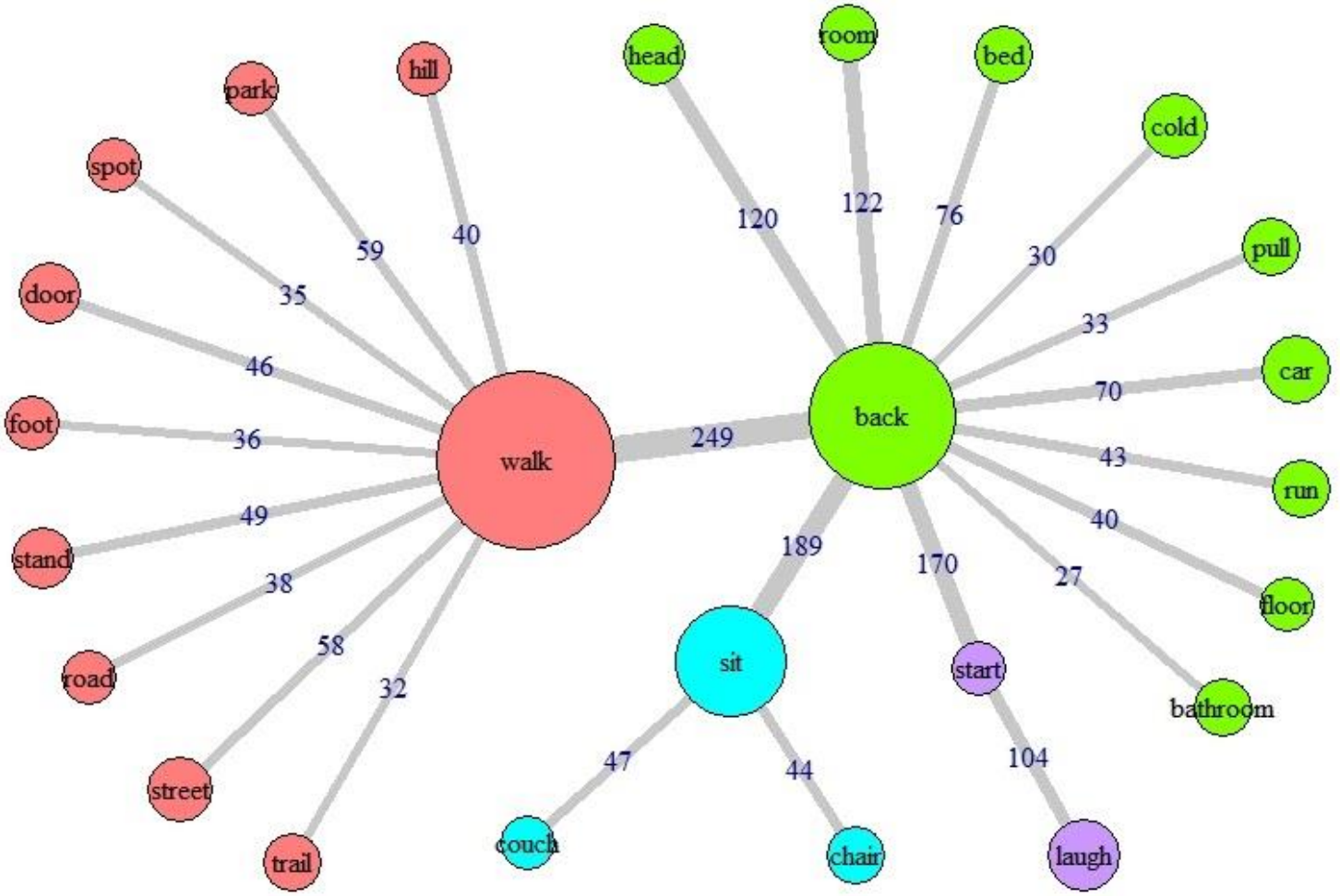


Figure 5 - **Co-occurrence and communities for words in cluster 3**

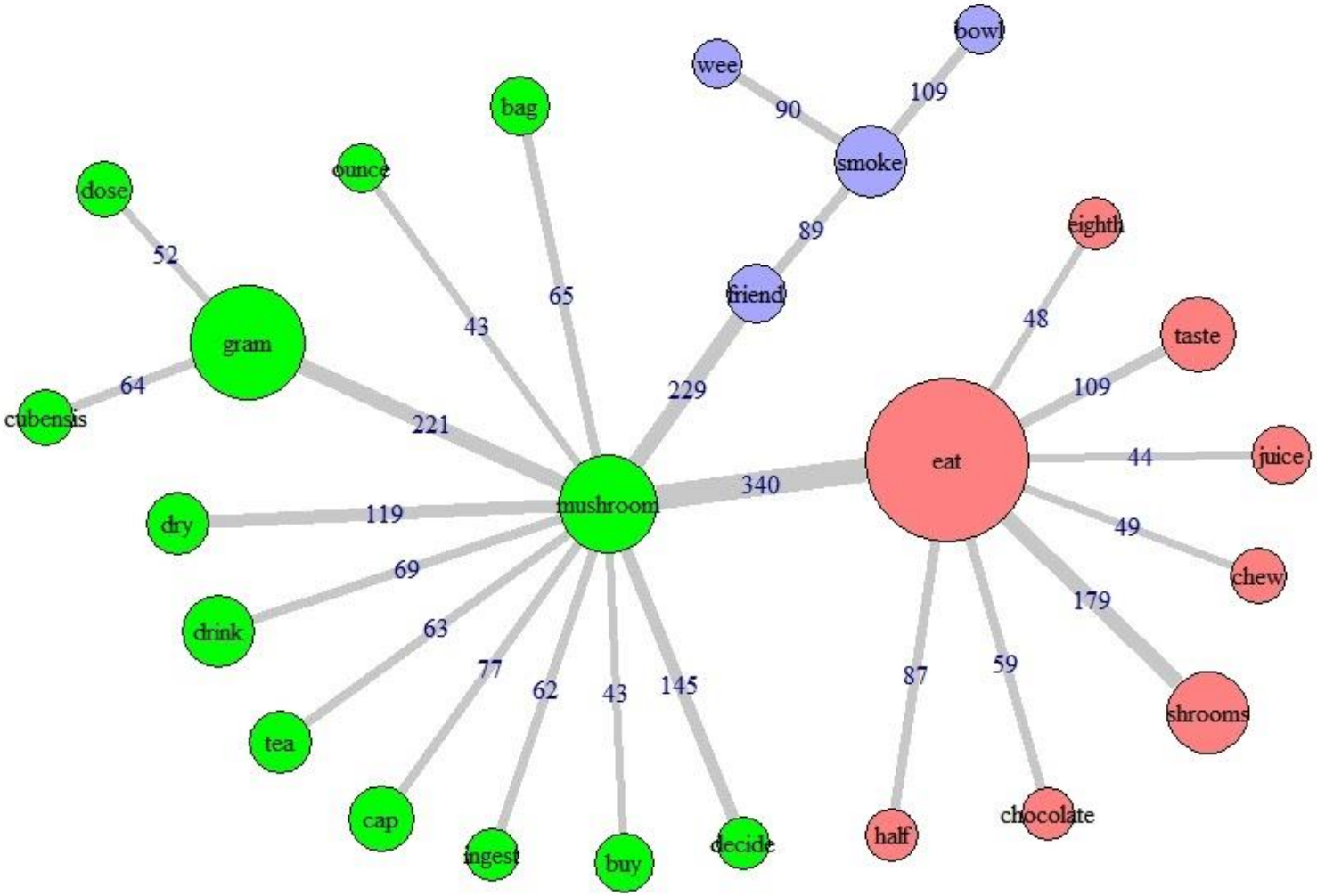


Figure 6 - **Co-occurrence and communities for words in cluster 4**

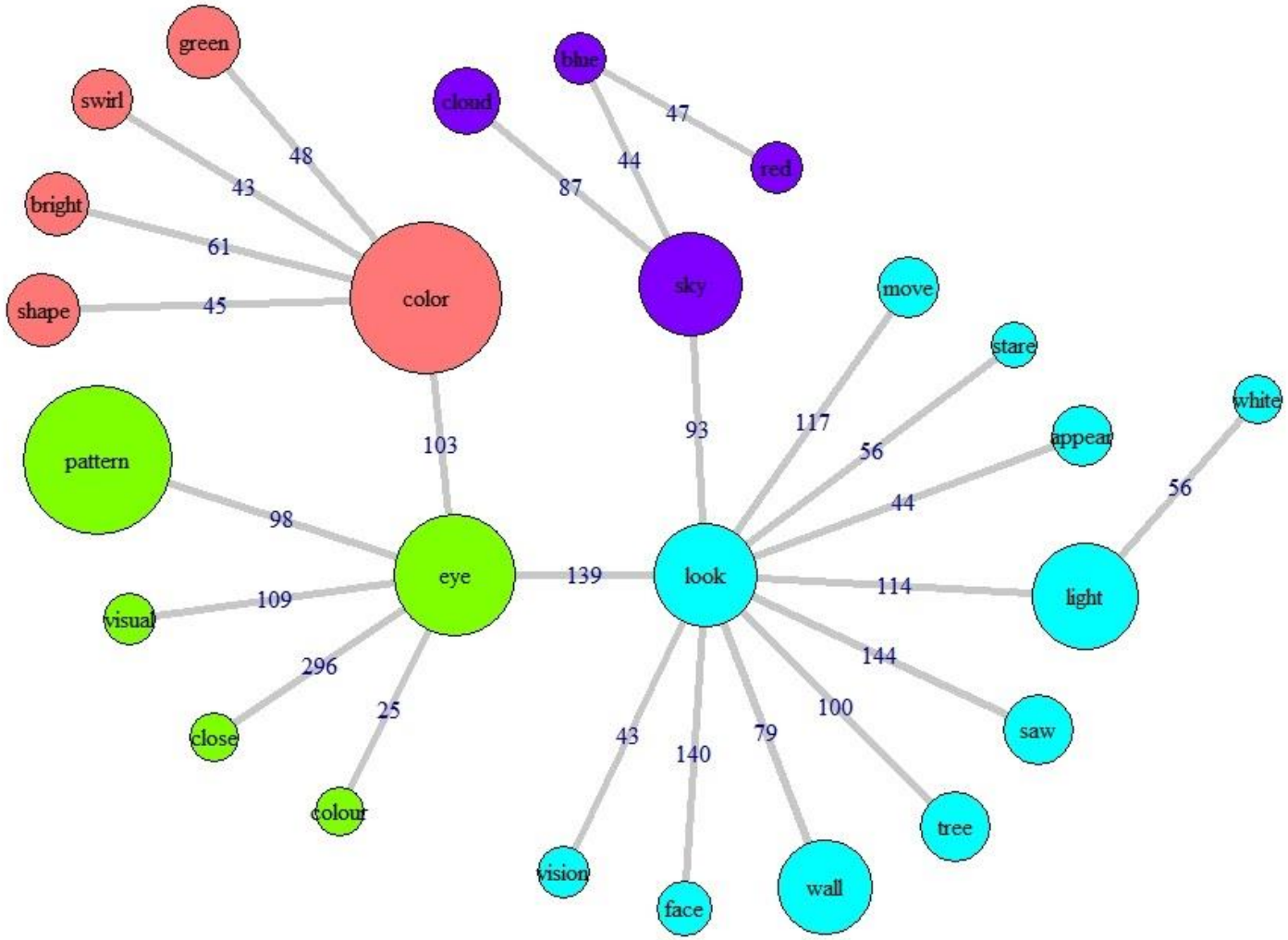
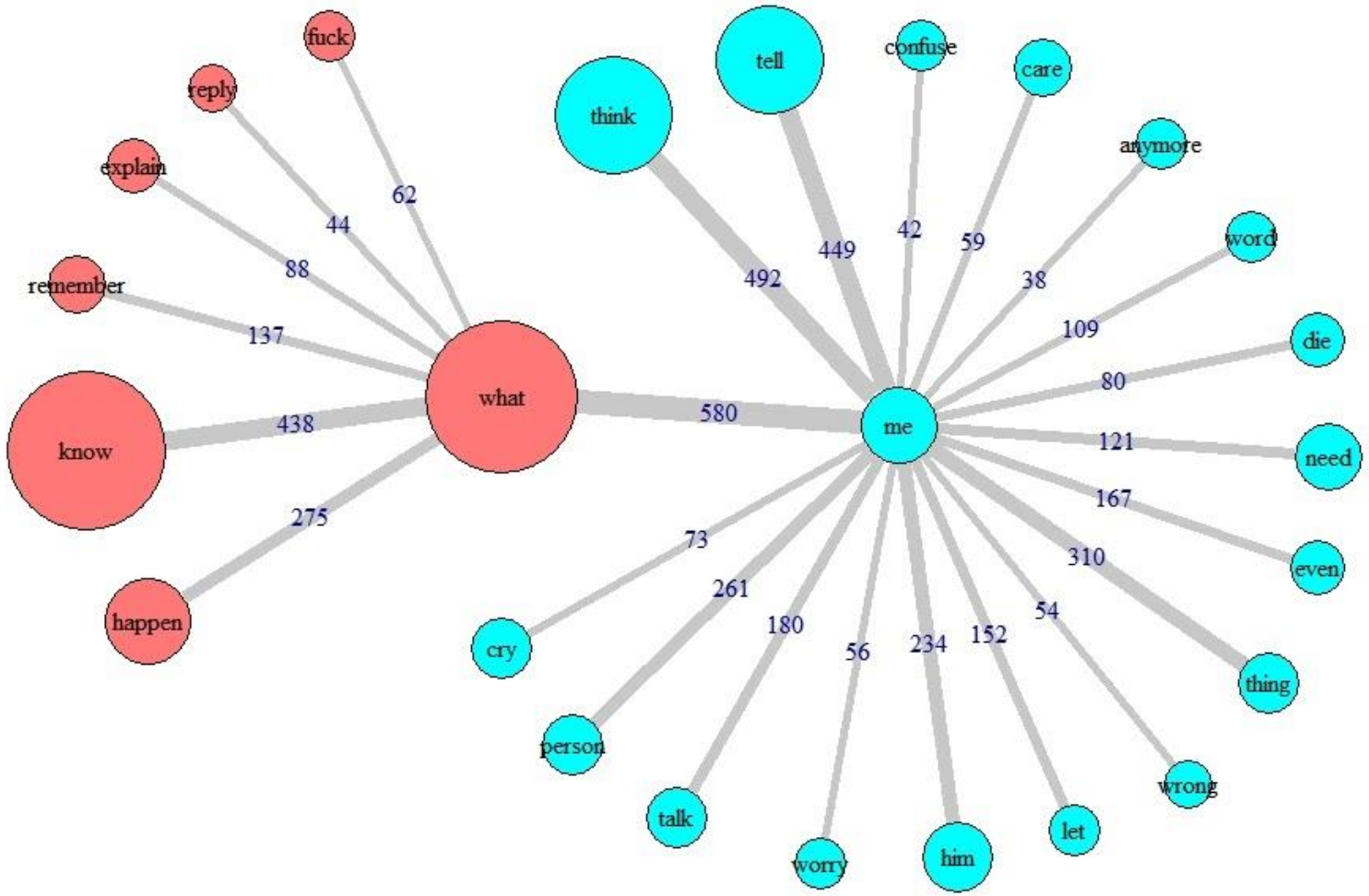


Figure 7 - **Co-occurrence and communities for words in cluster 5**



Discussion

The results indicated the occurrence of 5 clusters of words, that is, ‘environments of meaning’ present in the participants' speech (Salvador et al., 2018). A relationship can be seen between Clusters 1 and 5, with the words very close together on the AFC Cartesian graph (Figure 2), while Clusters 2 and 4 were slightly related, with the words close together on the same axis of the graph (Figure 2). Still in relation to the proximity of clusters, it is noted that Cluster 3 differs from the others both in the CFA graph (Figure 2) and in the dendrogram (Figure 1). When the clusters are analyzed semantically, the isolation of Cluster 3 makes sense, since it seems to concern the setting and the context in which the experience took place, while the others refer to contents arising from the experience itself. That is, while Cluster 3 gathers words external to the experience, the other clusters gather words more related to the first-person experience.

Analyzing the words individually and their associations with each other, it is assumed that Cluster 1, which included 24.1% of the TS, refers to the content of mental experiences typical of the experience with psychedelics, such as the ego-dissolution phenomenon (Letheby & Gerrans, 2017) and oceanic feeling (Preller & Vollenweider, 2016), with the presence of words such as “life”, “mind”, “universe”, “consciousness”, “nature”, “being”, “world”, among others. A similar cluster to this was also found in previous analysis of reports of negative experiences with psilocybin (see Bienemann et al., 2020). However, it is noted that, unlike the analysis of negative experiences, where words with negative connotations were also seen, such as "fear", "death", "insane", "crazy", "cry", "die", in this study, only positive and neutral valence words were present (with the exception of the word “death”, which appeared strongly linked to the word “life”). Thus, while the mental contents present in the reports of negative experiences approach a structure of negative affect marked by anxiety and paranoia (Kramer et al., 2014), in the reports of positive experiences the words make more reference to the phenomenon of ego-dissolution (Nour et al., 2016). This finding is in agreement with studies that show a positive correlation between ego dissolution and higher levels of life satisfaction, positive affect, among other positive mental health outcomes (e.g., van Oorsouw, 2021; Uthaug et al., 2018), which is also supported by the association of this cluster with the Health Benefits subcategory, although the association had a small effect size and was marginally significant ($p = .026$).

In addition, in this study, mystical words, such as “spiritual” and “jesus”, also appeared in this class, with a strong association of Cluster 1 with the subcategory “mystical experiences”. It is also noted, as seen in Figure 3, that the central and strongest word of this cluster was the word "life", and that there is a connection between the words "jesus" - "mind" - "life", as well as " spiritual” – “life” which, in turn, also connects to the word “existence”. That is, these associations give an auspicious connotation to mystical words, with more positive than a negative or anxiogenic sense. This fact is in accordance with data that point to mystical experiences as one of the possible elements that underpin the therapeutic mechanisms of psychedelics in mental health (Wheeler & Dyer, 2020). The strong association of this cluster with single doses may indicate the use of higher and more effective doses, which may be linked to the fact that psilocybin induces dose-dependent alterations in perception and positively experienced ego dissolution (Hirschfeld & Schmidt, 2021). While in a previous analysis of negative experiences (Bienemann et al., 2020) the cluster similar to this one was associated with bad trips and female users, in this analysis there was an association with health benefits and male users. It would be important for other studies to further investigate gender differences in the way of experiencing ego dissolution and other effects from stronger doses of psychedelics. It is possible that the effects of higher doses should be expressed more strongly in women, due to enzymatic, hormonal and even social factors.

Cluster 5 retained 22.5% of TS and was not associated with any subcategory. This cluster contains central words such as “what”, “me”, “know”, “think”, among others (Figure 7) and it was a cluster that did not appear in the analysis of bad trips. Some of the words in this cluster (eg, “think”, “know”, “remember”, “explain”) suggest a cognitive component to the experience with psilocybin. It is possible that this cluster is, in a way, part of the same environment of meaning as Cluster 1 because, in addition to being part of the same arm of the dendrogram (Figure 1), when we analyze the Corresponding Factor Analysis (Figure 2), we see that the words of these clusters seem quite close and related to each other. Therefore, possibly, it is a cluster that also relates to the mental phenomena typical of the psychedelic experience. However, unlike Cluster 1, this cluster included words that possibly demonstrate anxiogenic experiences, such as "cry", "confuse", "die", "worry", "fuck". These data demonstrate that even in psychedelic experiences with positive outcomes, there may be a difficult part of the experience that promotes some anxiety, but still contributes to the positive effects in general. This is in agreement with the literature

that reinforces that there is a therapeutic character in challenging experiences (Carbonaro et al., 2016), highlighting, however, the need for post-experience contextual integration work (Carhart-Harris et al., 2018) that can help integrating and making sense of the challenging narratives of users (Gashi, Sandberg, & Pedersen, 2021). Considering this, it would be important for further studies to seek to identify which subjective aspects during and after these experiences helped to transform them into positive outcomes.

The second cluster of words had 20.49% of TS and, as well as in negative-experiences analysis, showed terms related to action, such as "walk", "back" and "sit", which occupy central position in the cluster, with some nouns complementing it. The presence of positive terms, such as "laugh", and the absence of terms that appeared in the negative outcome analysis, such as "ambulance", "police", "hospital", "cop" (Bienemann et al., 2020), is also observed. Therefore, while in negative experiences some of these actions indicated a possible occurrence of emergencies (Bienemann et al., 2020), this nucleus does not appear in positive experiences. It is possible that this is explained by the association of this cluster with lower doses, leading to an experience that preserved functional capacity. Additionally, this cluster was strongly associated with glowing experiences, pointing to positive outcomes linked to somatic feelings. The occurrence of this cluster in both positive and negative experiences, albeit with different word associations, suggest that a bodily and motor component is central to psychedelic experiences.

This somatic component was closely linked to Cluster 4, which held 17.78% of TS, with words such as "color", "eye", "pattern", "look", "sky", among others, which refer to visual and perceptual changes characteristic of the psychedelic experience. This may suggest a strong perceptual core to subjective experiences of psilocybin users, encompassing both somatic and visual elements. This cluster was the most similar to the ones reported in the negative outcome analysis (Bienemann et al., 2020), with most of the words found here also having appeared for bad trips, highlighting the characteristic hallucinogen effects of psilocybin. In the current study, this cluster was associated with the "glowing experiences" subcategory, which may point to the fact that people who had this type of experience, and consequently registered them in this subcategory of the website, had more visual and perceptual changes in their experiences.

The third cluster held 15.08% of the ST and seems to be related to context and details of the experience in general, with words such as "mushroom", "eat", "gram", "smoke",

among others. A very similar cluster was also found in the previous analysis of negative experiences (Bienemann et al., 2020). In the previous study, words had appeared that indicated the use of other drugs along with mushrooms, such as "lsd", "acid", "weed", "marijuana", "pot", while in this study only the word "weed" appeared, related to "smoke" (Figure 5) which, in turn, relates to "friend". This reinforces the notion that the concomitant use of mushrooms with other substances can be harmful (van Amsterdam, Opperhuizen, & van den Brink, 2011).

Conclusions

This study aimed to analyze positive reports resulting from psilocybin consumption, from the perspective and words of the users themselves. Although psilocybin has been used for centuries, reports of subjective experiences of users are still seldom analyzed scientifically by researchers. We believe that these analyses reveal important mechanisms underlying the different possible outcomes that the same substance can promote in its users. Findings of this study reinforce central axes of the psychedelic experience (such as the presence of somatic and visual alterations, connectedness and feeling one with the world and effects of setting), as well as the beneficial character of the so-called mystical experiences that the substance promotes, and the importance of the ego-dissolution phenomenon when positively experienced. In addition, it reinforces the importance of studies aiming to investigate gender differences in psylocibin experiences, as well as exploring possible coping mechanisms to transform challenging experiences into beneficial experiences. It is possible that, in addition to integration work in post-psychedelic sessions, as several authors indicate, there are coping mechanisms that arise during the acute experience with the substance which may help in harm reduction initiatives and crisis management of people under the effect of psilocybin.

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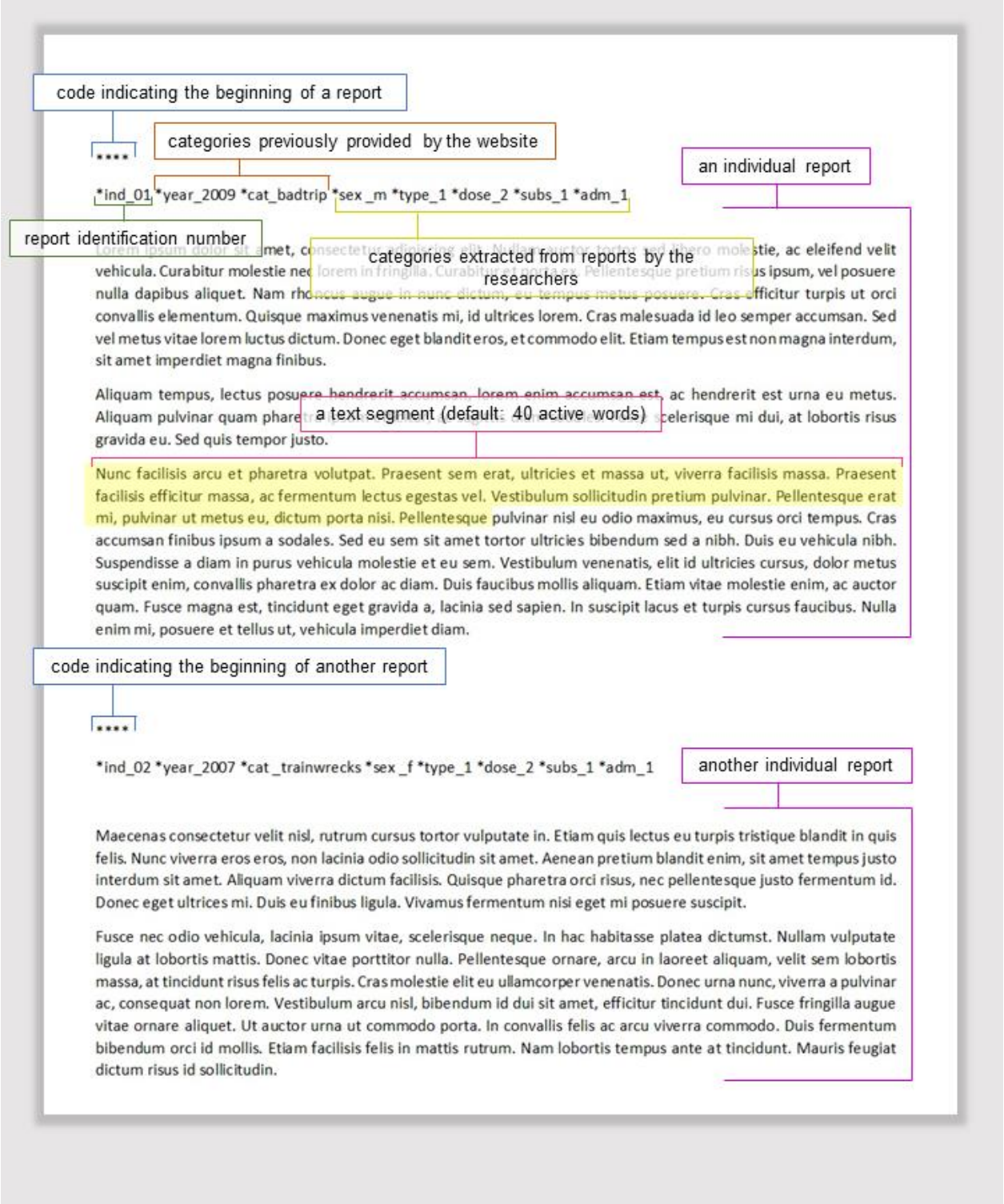
Supporting information

S1 Fig



ARTICLE 4

Bienemann, B. & Mograbi, D. C. Self-awareness, behavioural modernity and altered states of consciousness.

Abstract

The emergence of complex symbolic thinking and its products in human evolution, also termed behavioural modernity, is difficult to determine precisely. Prehistoric paintings found in caves are one of the oldest sources of evidence for human symbolism. This article aims to discuss and investigate: 1) human symbolic expression through prehistoric art, relating this with the development of self-awareness in our species; 2) the notion that cave paintings were part of broader ritualistic approach, including altered states of consciousness; 3) the hypothesis that altered states of consciousness, including those caused by psychoactive substances, are associated with the emergence of human symbolic expression. It is suggested that complex symbolic thinking, increased self-awareness and altered states of consciousness are interconnected in the history of human evolution. A blueprint for future research, drawing on disciplines such as cognitive neuroscience, comparative and developmental psychology, is suggested, aiming to explore the relationship between complex cognition, language, self-awareness and mental health, as well as how different methods of inducing altered states of consciousness can promote changes in gene expression.

Keywords

Self-awareness; palaeoanthropology; symbolic thinking; altered states of consciousness; psychedelics.

Introduction

Understanding what exactly constitutes humanity, what sets us apart from other forms of life, is a hotly debated topic. Exhaustive evidence indicates a line of continuity between humans and other animals, in accordance with a Darwinian theory of evolution, not only in physical, but also in cognitive or mental aspects. According to this gradualist perspective, evolutionary changes occur gradually over a broad scale of time, and the appearance of certain traits consequently follows a continuum over the course of evolution (Laland et al., 2015).

Self-awareness is the capacity of becoming the object of one's own awareness, implying a model of self that can be observed and that itself acts as the observer (Mograbi, Huntley & Critchley, 2021). It is possible that self-awareness is also not exclusively human, with evidence of a gradual continuum of this trait in other animals. Self-awareness can be thought of as a multi-faceted phenomenon, with components like interoception, metacognition, agency, proprioception, among others (for a review, Mograbi et al., 2021). Additionally, self-awareness has different levels of cognitive complexity. These levels vary across species considering not only the presence of specific components of self-awareness, but also the extent of their development or the awareness of this components (Lage, Wolmarans, & Mograbi, 2022).

Some cognitive features that were thought to be unique to humans have been observed in other animals, especially primates, such as perspective taking (Catala, Mang, Wallis, & Huber, 2017; Grueneisen, Duguid, Saur, & Tomasello, 2017), self-recognition (Huttunen, Adams, & Platt, 2017; Toda & Platt, 2015), metacognition (Beran et al., 2016; Couchman, Beran, Coutinho, Boomer, & Smith, 2012), anticipation and mental travel time (Roberts, 2007; Roberts, McMillan, Musolino, & Cole, 2012; Zentall, 2013). However, despite similarities between humans and other primates, there is a crucial disparity in relation to more complex aspects of self-awareness, linked to language development and complex symbolic thinking, leading to cultural accumulation in our species. It is not known exactly when in evolution this human capacity was consolidated, and there is also no consensus regarding its presence in other members of the genus Homo (Leary & Buttermore, 2003).

In a strictly adaptationist perspective, psychological mechanisms have evolved to solve some kind of specific problem, e.g. obtaining food, avoiding predators, or improving forms of social interaction (Haselton, Nettle, & Murray, 2015). For pioneers in the study

of evolutionary theory, the adaptive advantages that the sophisticated human mind could represent were a mystery (see Darwin, 1871; Wallace, 1870). It remains unresolved whether self-awareness is merely a consequence, i.e., a "side effect" of the evolution of brain complexity in humans, or if it is an adaptive ability itself (Haselton et al., 2015). Adaptive features of self-awareness would include decision-making processes assisted by interoception, theory of mind enabling great social interaction, self-recognition helping assessment of one's own health, metacognition promoting task performance, etc (Lage et al., 2022).

The temporal emergence of complex higher-order symbolic thinking and its products in the course of human evolution, so-called behavioural modernity, is hard to determine precisely. Given it is a first-person phenomenon, it cannot be read directly from the archaeological record (Miyagawa, Lesure, & Nóbrega, 2018), and it has been discussed whether it was a discontinuous or gradual process (Tattersall, 2017). Prehistoric paintings found in caves are one of the earliest forms of evidence of human symbolism (Clottes et al., 1995). Initially, the archaeological record suggested that the emergence of this type of expression was exclusive to Homo sapiens due to its co-occurrence with jewellery, decorative objects, paintings and other symbolic artefacts found in European caves dating back to 40,000 years ago (White, 1992). However, recent discoveries found in Iberian caves about the symbolic use of shells and pigments dating back more than 150,000 years ago seems to indicate that such capacity probably also existed in Homo neanderthalensis (Hoffmann, Angelucci, Villaverde, Zapata, & Zilhão, 2018). Regardless of their specific origin, evidence is conclusive in indicating that only members of the genus Homo with more advanced cognitive abilities were capable of cave paintings.

There are many studies that seek to understand the content of many of these art forms (for a review, see Clottes, 2008; Valladas et al., 2001). Many paintings seem to be representations of human daily life (e.g. hunting), while others represent monothematic and exhaustive depictions of a certain theme (e.g., horses) or atypical mystical figures (e.g. bee-faced shaman found in cave paintings at Tassili n'Ajjer). Furthermore, there is evidence that some paintings are placed considering the acoustic characteristics of the chambers where they are localized (Miyagawa et al., 2018). This suggests the idea that these paintings were part of festive or ritualistic events.

Considering this, the current article explores human symbolic expression through cave and rock art, relating this with the development of self-awareness in our species.

Additionally, the notion that cave paintings were part of broader ritualistic approach, including altered states of consciousness, is discussed. Finally, the hypothesis that altered states of consciousness, including those caused by psychoactive substances, are associated with the evolution of symbolic expression in our species is revisited.

Complex symbolic thinking in Homo sapiens and self-awareness

It is considered that Palaeolithic cave art is an externalized and fossilized form of language, a concrete expression of an internalized system of thought (Miyagawa et al., 2018). In this sense, cave art would be evidence of the complex symbolic and visual representation capacity of their authors. Some archaeologists consider "art" an inappropriate term, preferring to name the cave signs by the term "graphisms", suggesting that in simpler societies these representations are related to the routine of communities, traditions, rituals, and not necessarily for pleasure or contemplation as Anthropocene art (Gaspar, 2003).

The ability of creating visual art or graphisms is one of the defining characteristics of the human species, but it is hard to determine the starting point of these representations during our evolution. For a long time, the palaeoanthropology community has primarily focused on Upper Palaeolithic European rock art (paintings), as well as 3D figures (sculptures), such as fertility doll-like Venus figurines (Morris-Kay, 2010). These figurines are carved statuettes portraying women with emphasised female features (Fagan & Beck, 1996; see Figure 1 for an example). Sophisticated examples of Palaeolithic art can also be seen in paintings from European sites like Altamira, Dordogne and Ariège, for example, dating back to 17,000 years ago, and even older paintings like those found in Chauvet's Cave dating to 30,000 years ago (Valladas et al., 2001).

However, recent excavations have provided evidence that the emergence of complex symbolism may be even older. For example, fragments of intentionally marked ostrich eggshell containers dated to 60,000 years ago were found at Diepkloof Rock Shelter (Texier et al., 2010) and considerable evidence has been recovered from Blombos Cave dating to around 75,000-100,000 years old, such as geometric engraved ochres (Henshilwood, d'Errico, & Watts, 2009), tools having grooves and patterns supposedly made by pressure flaking technique (Mourre, Villa, & Henshilwood, 2010) and abstract drawings (Henshilwood et al., 2018). In Blombos Cave, more than 8,000 pieces of ochre-

like material supposedly manipulated by Homo sapiens have been found (Rosso et al., 2017). These South Africa excavations have provided powerful insights about symbolic activity and art techniques, such as the use of colours, pattern development, engraving, use of bone and rock materials, etc. Figure 2 depicts some of these symbolic expressions from European and African sites.

Figure 1 – Venus figurines

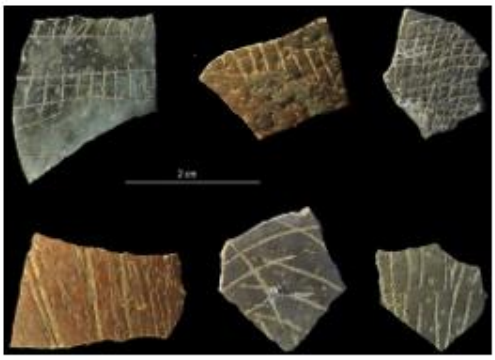
(Credit: Natural History Museum Vienna)

Figure 2 – Archaeological findings from European and African sites

1 - Bison depicted at the Altamira cave in northern Spain

Photo by: Thom Quine

3 – Fragments of engraved ostrich found at Diepkloof Rock Shelter

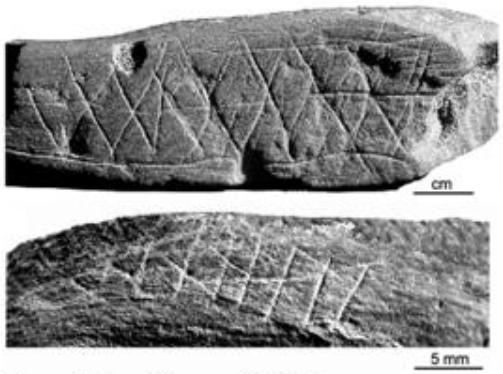


From: Texier et al., 2013.

2 - Cave paintings in the Chauvet Cave.

Photo by: AFP

4 – Engraved ochres founded at Blombos Cave



From: Henshilwood, 2007.

While the cognitive ability to create art probably originated in Africa, cradle of anatomically modern humans, the practice itself may have started at different times among different groups of individuals, with both genetic and cultural differences expected (Morris-Kay, 2010). Different aspects can be analysed to determine the complexity of a graphism, such as the use of colours, the applied graphic patterns, how 2d or 3d images are started, material or surface used, the modification of natural shapes, among others. The complexity of these aspects seems to be related to the progression of cognitive abilities in our species, providing a reference of the system of thought and cognitive level of artists (Miyagawa et al., 2018). A human being with these art abilities must have had

some basic cognitive competences. For example, memory is needed to retain the images to be drawn and recall these representations; selective attention allows suppression of potential distractions during the course of work; symbolic thinking provides the capacity to represent images internally and retain or change their meaning (Gray, 2010). Additionally, it is hypothesised here that self-awareness may also have been a crucial ability for the development of prehistoric art.

As indicated above, self-awareness can be defined as the capacity to become the object of one's own awareness, implying a self-model that can be observed and that itself acts as an observer (Mograbi, Huntley & Critchley, 2021). In a rudimentary form, self-awareness may be seen even in very simple organisms, for example when accessing internal states and using the available information to take decisions (Budaev et al., 2020). Nevertheless, self-awareness may have different levels of cognitive complexity. It is possible that more recursive forms of self-awareness, i.e., those that not only represent internal states but manipulate this self-representation, are only seen in primates.

One example of a self-awareness component varying in complexity across species is theory of mind (ToM). ToM is the ability to attribute mental states to others, representing what others perceive, feel and know (Carlson, Koenig, & Harms, 2013). It is linked to self-awareness because in order to infer others' mental states, it is necessary to understand that one's own mental states and inferences impact behaviour (Lage et al., 2021). A simple way of achieving that is by simulating others' mental states in our minds, which relies on a representation of our own mental states. This has been termed a simulation approach to ToM, and it is considered a less complex form of ToM, as opposed to "theory theory" perspectives, which suggest that not only others' mental states are simulated, but that a theory about them can be developed (Roska-Hardy, 2009). ToM has been observed, at least partially, across phyla such as Arthropoda, Mollusca and Chordata, suggesting that its simplest form (i.e. simulation) may be present through homology in very diverse species. However, given less consistent results in studies exploring these abilities in animals other than mammals, it has been suggested that more complex organisms may also rely on inferences and knowledge, explicit or implicit in nature, to predict mental states of others (i.e. developing an actual theory). This points to an inflection in the level of complexity of this self-awareness ability in the course of species evolutionary pathways. Other self-awareness abilities may have gone through similar processes,

accumulating complexity in species with more developed nervous systems (Lage et al., 2021).

Art needs some level of self-awareness, quite possibly a fairly complex one, loaded with recursive abilities. Distinct self/other images are represented mentally, manipulated and graphically displayed in different material substrates Detailed depictions of human figures, such as Venus engravings, indicate that authors have developed distinct awareness of the human body and reconstructed it through a symbolic representation of salient features. Furthermore, there is a considerable amount of art on cave walls representing humans in first- (e.g. handprints) and third-person perspectives (hunting scenes), providing direct evidence of the capacity of self-awareness of its authors (Pizzato, 2013).

Hypotheses for the emergence of behavioural modernity

The spatio-temporal diversity of cave and rock graphisms indicates that these forms of art did not necessarily follow a linear or gradual path in course of evolution. This is expressed in different forms of art recovered from distinct periods around the world. Some authors argue that technological and symbolic innovations in human evolutionary history represents a drastic and qualitative change in behaviour, consequently signalizing the emergence of symbolic thinking (Miyagawa et al., 2018). Others, however, propose that this process was more gradual and continuous, with change accumulating slowly through time.

At the centre of this debate is a debatable time gap between the emergence of anatomically-modern humans and so-called behaviourally-modern humans. The hominid brain reached almost its present size about 250,000 years ago (Kaas, 2013), but many of the cognitive attributes considered uniquely human seemed to be appeared only much later. Moreover, Neanderthals had a brain that was larger in volume than humans (Holloway, 1981) but did not develop the kinds of behaviour associated with higher cognitive ability, such as such as language, commerce or agriculture (Miyagawa et al., 2018).

It is known that before the Pleistocene period the technological innovation was limited, with long time stretches during which very few changes in human-made tools occurred

(Tattersall, 2017). For example, the first stone-tool technology appeared 2.5 million years ago and did not change for a million years before innovation was introduced in the form of the Acheulean hand axe (Semaw et al., 1997). However, toward the end of the Pleistocene, technological innovations began to appear in rapid progression, especially with improvement of hunting techniques and an explosion of tools made with bones (Rabett & Piper, 2012). This period of rapid change also corresponds approximately to the artefacts recovered from Blombos Cave, which have been considered markers of symbolic thinking (Miyagawa et al., 2018). This rapid progression on technological innovation may indicate an abrupt and qualitative change in human mental information processing (Tattersall, 2017).

Those that favour a gradual approach point both to a paucity of the fossil record and consistent evidence from Africa to suggest that behavioural modernity accumulated slowly and initiated earlier than previously suggested. For instance, Sahle and colleagues (2013) indicate that stone-tipped projectile technology was already available at least 279ka in the Ethiopian rift. Brooks et al. (2018) report pigment use and long-distance transport of stone-materials in South Kenya dating around 300ka. Altogether these suggest that early signs of behavioural modernity are present at the sites were some of the first anatomically-modern humans were found. It has been suggested that behavioural-variability is a more fruitful approach to understand human evolution than the concept of behavioural-modernity (Shea, 2011).

Discontinuous explanations suggest that certain features and events may have promoted drastic changes in human symbolic capacity. For instance, beyond brain sizes, the functionality of brains may have continued to evolve after the emergence of anatomically-modern humans. One explanation may be the possible increase in number and refinement in function of mirror neurons on the human brain, allowing humans to read and understand another's intentions, and develop a sophisticated theory of other minds (Ramachandran, 2012). The development of language may have altered the brain white matter microstructure (Cheng et al., 2019), changing the number of synapses and neuronal connectivity within the human brain. Another interesting fact is that the human brain has shrunk by 13% in the last 20,000 years after having grown continuously during the Pleistocene (Hawks, 2011), which may be linked to differences in dealing with information, provided by symbolic thinking development.

Symbolic thinking, i.e., the ability to internally represent something, along with its associated meaning, probably has a relation with language development. Both language and cave art required creativity and symbolic thought processes and there is good evidence for a neurological relationship between visual creativity and language (Miyagawa et al., 2018). In this sense, it is possible that these two phenomena are related in the history of human evolution. It is possible they appeared around the same time, predating the migration out of Africa (Huijbregts, 2017), and representing externalized internal mental states.

Molecular biology and genetics can also provide explanations for the development of language and symbolic thinking. The gene 'FOXP2', for example, was discovered by empiric studies as essential for language acquisition (Lai et al., 2001). It encodes a transcription factor, a protein that binds to DNA and helps determine the level of expression of other genes. Experiments have shown that the human version of this gene, which has two different amino acids compared to the version carried by chimpanzees, has different effects on genes, potentially affecting brain development and explaining why only humans are capable of complex language (Smith, 2009). Mutations of this gene in humans has been found to underlie a severe developmental disorder that significantly disrupts speech and language skills, with impacts on orofacial motor control and synaptic plasticity of neural circuits (Fisher & Scharff, 2009). It has also been implicated in conditions such as schizophrenia and mood disorders (Li et al., 2013). Given the similarity between language and art, it has been suggested that a shared genetic change may have given rise to the multi-modal art that occurred all over the world alongside language (Miyagawa et al., 2018). However, the human variant of this gene seems to not differ at all in Neanderthals (Hauser et al., 2014). Human FOXP2 has been the target of selection during recent human evolution and probably explain in part the emergence of language, but it is certainly not the only determining aspect.

One alternative hypothesis for the development of human symbolic thinking is presented by McKenna (1992). According to him, indole hallucinogenic substances played a decisive role in the emergence of human self-awareness and complex symbolic thinking. Nevertheless, this hypothesis is fraught with inconsistencies, ranging from a misunderstanding of the mechanisms of evolutionary change and heritability to the lack of availability of certain hallucinogenic species in Africa. In the next section, McKenna's ideas will be revisited, exploring its rationale and discussing whether a modified version,

considering recent knowledge of evolutionary mechanisms and a broader view of altered states of consciousness, can lead to testable empirical predictions and progress in the understanding of human self-awareness.

Revisiting the Stoned Ape Theory

Amongst the different hypothesis for a discontinuous appearance of rich symbolic thinking in Homo sapiens, McKenna's (1992) is remarkable in that it relates this phenomenon with the use of psychoactive substances. According to him, psychoactive substances caused mutations that led to the reorganization of the processing abilities of the brain. In its most specific formulation, McKenna argues that the consumption of psilocybin – the active ingredient in magic mushrooms – by hominids may have had an impact on the sudden emergence of higher-order consciousness and language. Two main points are suggested as sources of support for his hypothesis: geographical availability and the subjective effects of psilocybin.

In relation to geographical availability, psilocybin is proposed after considering requirements that a hallucinogenic plant or fungus would have to meet to thrive in prehistoric Africa. Psilocybin-containing mushrooms are pantropical, relying on saprotrophic nutrition, i.e. growing on decaying organic matter. They are commonly found in America, but have also been recorded in Europe (Borovička, Noordeloos, Gryndler, & Oborník, 2011), Asia (Allen & Merlin, 1992) and Africa (Nkadimeng et al., 2020). According to McKenna (1992), mushrooms would be the hallucinogenic species most likely to be found in the African prairies by a hunter-gatherer society, being more ubiquitous in that specific historical context.

Regarding the subjective effects of psilocybin, according to McKenna it would lead to states of self-reflection not experienced before by early humans. This would promote increased linguistic ability, contributing to more complex social relationships, and foster the development of imagination. At lower doses and intermediate doses, psilocybin would cause increased visual acuity and sexual activity, with survival and reproductive value respectively. At higher doses, psilocybin can promote alterations of consciousness that are expressed as an oceanic feeling, a sense of connection with the whole and greater proximity to nature (Martial et al., 2021; Nour, Evans, & Carhart-Harris, 2017); a phenomenon commonly referred to as "ego dissolution" (Nour et al., 2016). As indicated

previously, self-awareness can be defined as a recursive trait, the capacity to self-reflection, that implies a self-model that can be observed and that itself acts as an observer (Mograbi et al., 2021). Psychedelics can change self-awareness by alterations that disrupt neural networks implying self-reference (Letheby & Gerrans, 2017) and stimulate autobiographical memory (Healy, 2021).

There are a number of inconsistencies in McKenna's hypothesis. In relation to geographical availability, although there are some records of mushrooms containing psilocybin in Africa, data regarding the probable availability of these mushrooms in that region during prehistorical times are still inconclusive. Currently, there are approximately six species of *Psilocybe* in Africa, the least studied continent from a mycological point of view (Froese, Gúzman, & Gúzman-Dávalos, 2016). In Ethiopia, home of some of the most relevant fossils of anatomically modern humans, there are records of *Psilocybe cyanescens* and *Psilocybe merdaria* founded in dry Afromontane forests and *Eucalyptus grandis* plantations (Dejene, Oria-de-Rueda, & Martín-Pinto, 2017a; Dejene, Oria-de-Rueda, & Martín-Pinto, 2017b). However, it is unlikely that humans at that time would have lived in the forest, considering the danger of such an environment. An alternative would be mushroom consumption of species born from cattle dung in open areas. McKenna suggests that domestication of wild cattle would have facilitated this process. Nevertheless, this creates a temporal inconsistency, given that cattle domestication occurred through a number of events that happened in the past 10.000 years (Pitt et al., 2019), thus not fitting with the timeframe for the emergence of complex symbolic thinking in humans and also happening well after the migration of sapiens to regions outside of Africa.

Regarding subjective effects, although psilocybin can promote a number of potential beneficial effects, with growing evidence on mood improvement (Nichols, 2020), a main issue refers to how these effects would be transmissible to offspring. In other words, even if psilocybin consumption could lead to more adaptable phenotypes, with transient increased fitness, these characteristics would not be passed on to progeny. McKenna (1992) seems to realise this flaw in his proposal, by questioning whether it would amount to Lamarckism. According to him, one solution for this issue is to consider that transmission could have occurred socially, through cultural habits. He discusses the possibility of changes in consciousness bringing new behavioural patterns that would be beneficial to society, such as increased reliance on language. Nevertheless, this only shifts

the issue of selection to a group level. The concept of group-selection in evolution has been extremely contentious (Zywicki, 2000), with many claiming it does not have a place in modern evolutionary theory (Dawkins, 1989; Pinker, 2015).

Can a reformulated version of McKenna's hypothesis provide a more cogent narrative for the evolution of human self-awareness, while also generating testable empirical predictions? In order to advance this proposal, alternatives for the inconsistencies in geographical availability and transmission of subjective effects are needed. For this purpose, two main ideas are suggested: (1) considering a broader perspective on altered states of consciousness, going beyond psilocybin, for which geographical availability seems very limited; (2) exploring epigenetics as a potential mechanism for transmission of changes induced by altered states of consciousness

As indicated previously, some evidence suggests that prehistorical cave paintings were placed strategically, considering the acoustic characteristics of the chambers in which they appear (Miyagawa et al., 2018). This could be suggestive that either the act of painting or the subsequent relationship with the decorated environment could have been linked to ritualistic purposes. This is reinforced by the perceived symbolism in cave art and analogous prehistorical representations (such as sculptures). Guthrie (2005) draws attention to the lack of narrative that existed in many of these artistic expressions. Clottes (2008) indicates that there is a very limited number of paintings of landscapes, small animals, insects, plants, or even close people, children, or other realistic human representations. Altogether this suggests the symbolic nature of these expressions.

Anthropological studies suggest that altered states of consciousness are a fundamental part of the beliefs systems of a very large proportion of traditional societies (Guerra-Doce, 2015). In a vast survey, Bourguinon (1973) indicates that 437 out of 488 (90%) traditional societies incorporate altered states of consciousness in the formation of their ritualistic/religious behaviours and worldview beliefs. Altered states of consciousness can be achieved through a variety of ways, including sensory stimulation/deprivation (e.g. chants, isolation, lack of visual stimulation), physiological deprivation (e.g. food, water, sleep deprivation), exposure to environmental extremes (e.g. hot or cold temperatures), physical exertion, meditation, breathing techniques, and the consumption of psychoactive substances (Wittman, 2018).

There is some evidence, albeit limited, for the relationship between altered states of consciousness and cave art in a comparative anthropology approach. Lewis-Williams & Dowson (1988) apply a neuropsychological model of altered states of consciousness to current shamanistic rock art from traditional African and North-American societies, identifying recurring patterns that are also observed in Upper Palaeolithic art. This suggests that, indeed, this art was also associated with altered states of consciousness. These would lead, especially in the context of religious rituals, to transcendent experiences and the possibility of seeing ourselves from a different perspective, which is a crucial element in more complex forms of self-awareness.

Considering altered states of consciousness in a broader manner mitigates one of the central difficulties of McKenna's hypothesis, the lack of consistent evidence for the availability of psilocybin, and hence its consumption, by early anatomically-modern humans. Given the plethora of methods to induce altered states of consciousness, some of which can be involuntarily occurring due to sensory or physiological deprivation, the need for a specific psychoactive substance is reduced. This broader perspective thus acknowledges that altered states of consciousness were an integral part of rich symbolic expression in humans, whilst not relying on the existence of psilocybin sources in the African continent.

This leaves, however, another major hurdle in the theory, namely how any changes induced by altered states of consciousness would be transmitted to offspring. One alternative is to consider epigenetic transmission. Although there is brief mention by McKenna (1992) of epigenetics, this is never fully explored and it is not clear the meaning and understanding that the author attributes to the term. Epigenetic can be defined as modifications in genetic material that change gene expression, without altering the genes themselves (Carey, 2011). Although epigenetics has been studied for decades (see Waddington, 1942), only more recently research has explored how phenotypical changes caused by epigenetic mechanisms can be transmitted to offspring. This has led to a shift in the definition of epigenetics as a field of knowledge concerning alterations in gene function that are heritable, mitotically or meiotically, without changes in DNA sequence (Dupont, Armant & Brenner, 2009).

Epigenetic mechanisms, such as DNA methylation and histone modifications, have been implicated in changes in mental functioning (for example, being liked to psychiatric disorders; Karsli-Ceppioglu, 2016; Klengel et al., 2014; Tsankova et al., 2007) and are

known to be particularly responsive to environmental change. For example, exposure to childhood maltreatment has been linked to alterations in gene expression (Vijayendran et al., 2012), epigenetic differences accumulate over the life course of monozygotic twins, especially when they are exposed to different environments (Fraga et al. 2005), and food deprivation – which as indicated above can lead to altered states of consciousness – is linked to changes in epigenetic patterns (Haggarty, 2013). Thus, the relationship our ancestors established with their environment, including through the induction of altered states of consciousness, may have caused changes in gene expression. The extent to which these alterations would be passed on to offspring is still debatable, with more evidence for epigenetic transmission in plants than in mammals (Heard & Martienssen, 2014). In any case, identifying epigenetics as a potential mechanism for the inheritance of environment-mediated changes in humans is one of the ways to avoid Lamarckism in McKenna's hypothesis.

Conclusions

In summary, it is our contention that complex symbolic thinking (represented by cave art), increased self-awareness (with expanded recursive features) and altered states of consciousness are linked in the history of human evolution. In considering this hypothesis, we are not inferring a specific direction of causality, but rather suggesting an ensemble of characteristics that are correlated, being hard to ascertain what emerged first, causing other characteristics. Although this may reduce the impact of the hypothesis, there is an important precedent for a similar approach in palaeoanthropology, not least in the emergence of the genus Homo. It is known that a number of characteristics such as reduction of post-canine dentition, introduction of animal protein in our diets, increases and brain size and tool use have appeared within close proximity in the fossil record (Park et al., 2007). There is no consensus on whether tool use facilitated access to protein sources, allowing better nutritional resources and changes in brain size and dentition, or if there is another direction of causality, with brain size preceding and allowing tool use, which in turn led to changes in diet (Burini & Leonard, 2018). In any case the overall picture is that these abilities emerged together. Similarly, we are suggesting that behavioural modernity, self-awareness and altered states of consciousness are part of an evolutionary ensemble.

Our hypothesis does not imply a sudden emergence of behavioural modernity. Given the debate surrounding whether behavioural modernity is gradual or represents a discontinuity (Laland et al., 2015), it is important to highlight that the development of self-awareness, and rich symbolic thinking through altered stated of consciousness may have been the effect of accumulated changes through time or due to a more sudden discontinuous process. Ultimately, the answer to this question lies on future discoveries in the fossil record, with intermediate expressions supporting a gradual view and accumulated artefacts from specific periods pointing to discontinuity.

This revisited perspective generates a number of empirically testable hypotheses. Further anthropological and historical evidence can illuminate the relationship between ritualistic approaches and altered states of consciousness in contemporary and ancient traditional socities. A large number of extant ritualistic approaches not involving altered states of consciousness would help falsifying our approach. Additionally, a research programme exploring how different methods to induce altered states of consciousness may promote changes in gene expression would be capable of revealing important processes for further investigation, that could be explored in relation to complex cognition, language and mental health. Lack of epigenetic change after altered states of consciousness would falsify the current hypothesis. Finally, research into self-awareness, language and complex symbolic thinking in humans, relying on disciplines such as cognitive neuroscience, comparative and developmental psychology, would shed light on the relationship, if any, between these constructs.

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IV. General discussion

The general objective of the present thesis was to explore different aspects of psilocybin consumption, including the ego dissolution phenomenon, positive and negative outcomes perceived by users themselves, and the hypothesis that altered states of consciousness, including those caused by psychoactive substances, are associated with the emergence of human symbolic expression. In this context, our study aimed to contribute with a better understanding of the mechanisms underlying the outcomes of psychedelic use, particularly of psilocybin.

In the first article, the aim was to adapt and initiate the validation process of the Ego Dissolution Inventory (Nour et al., 2016), an instrument globally used to measure the ego dissolution experience. Although the scale showed solid psychometric properties and excellent internal consistency, items did not replicate the original structure. The more acceptable solution showed a tri-factorial structure, where items coalesce in aspects related to self-confidence and assertiveness, ego dissolution and ego inflation. The self-confidence and assertiveness factor included items that were originally considered as part of ego dissolution and inflation. This may suggest that ego effects must be considered beyond the dissolution/inflation dichotomy. For instance, perhaps there are states of dissolution of the self that retain some elements previously considered as representing inflation. Thus, a scale that aims to measure ego alterations must consider the multiplicity of components that constitute this construct, in line with the hypothesis that self-awareness is a multi-component phenomenon (Mograbi et al., 2021).

In the second article, we aimed to investigate psilocybin users' self-reports of negative outcomes, with positive outcomes being covered in the third article. The results indicated a similar structure for both negative and positive analysis, revealing clusters about mental quality of the experience, perceptual alterations, bodily and motor component of the experience and the context of administration of the substance. A main difference between the analysis of bad and positive experiences is that thoughts about the experience were divided into two different related clusters in positive outcomes. While in the second study of the thesis, speech analysis revealed terms related to an anxiogenic experience of ego-loss grouped in one cluster, in article 3 terms referring to this mental phenomenon were divided into two clusters: the first with reflexive words, such as 'life', 'world', 'nature', 'mind', 'love'; while the second showed a structure more similar to the one revealed in

the analysis of negative outcomes, with words such as ‘what’, ‘me’, ‘think’, ‘know’, in association with words that convey a notion of anxious states, such as ‘confuse’, ‘cry’, ‘worry’, ‘die’, among others. The other clusters presented very similar structure in both analysis, showing the following themes: perceptual alterations (focusing in visual elements), bodily and motor component (referring to acts and verbs that convey movement), and aspects related to the set and setting of experience.

Ego-dissolution is one of the main features of the psychedelic experience (Nour et al., 2016) and it is a subjective effect that is believed to be closely related to the positive clinical outcomes promoted by psychedelics (Uthaug et al., 2018). However, there seems to be an anxiogenic aspect in ego-dissolving experiences. Anxiety is a useful trait, shaped by natural selection, helping organisms to activate and defend themselves against a variety forms of threats (Marks & Nesse, 1994). Thus, it makes senses that in the presence of a threat – in this case, ego-death –, the organism triggers an anxiety response, and perhaps this response also expresses itself as enhanced self-reference. In other words, under a psychodynamic framework, in an attempt to preserve itself, maybe the ego increases self-reference, leading to a negative experience composed by self-related fears, such as the fear of going insane, out of control or dying.

Considering this, mystical experiences may be some of the subjective responses attributing meaning to the feeling of disintegration. This phenomenon resembles the cognitive model of delusions presented in psychotic disorders like schizophrenia, where the aberrant beliefs are hypothesized to arise from an effort to seek meaning in inner or outer experiences that are unusual, abnormal, or emotionally significant (Freeman, Pugh, Vorontsova, Antley, & Slater, 2010). In addition, recent data suggest connections between mystical experiences, ego-dissolution and aberrant salience, pointing to shared mechanisms both for psychotic and psychedelic experiences (Wießner et al., 2022).

Delusions can help making sense of unusual experiences, and it has been hypothesized that they may have an adaptive role, providing a defensive and palliative function (McKay, Langdon, & Coltheart, 2010). They can also reinforce the feeling that one's life has meaning, which may promote a positive sense of agency and creativity for the individual (Ritunnano & Bortolotti, 2021). Converging with this, subjective effects of psychedelic experience, such as ego-dissolution/ mystical experiences, may also be a mechanism to attribute meaning to the alterations caused by psychedelics. Given previous reports that attributing meaning to the psychedelic experience can be associated with

positive health outcomes (Carhart-Harris et al., 2018), it is possible to speculate that a difference between negative (such as delusional defenses) and positive outcomes (health benefits) refers to the extent to which meaning is attributed and also other cognitive attributes (e.g., self-referential thinking) and risk factors.

Another aspect of these experiences is the relation between ego-dissolution and transcendence, with a reduction in self-referential processing. This notion is particularly important in relation to the development of symbolic thinking in Homo sapiens (fourth article). The experience of ego-dissolution leads to a disconnection of the self and, instead, its observation from an external perspective. This may have helped the development of recursive first-person experiences, fostering more complex forms of self-awareness. The transcendent experiences promoted by altered states of consciousness may be also related to ritualistic and religious aspects, being a constitutive element of them.

The explosion of human symbolic expression may be related with positive aspects of a structured and refined self, but also with the suffering resulting by recognising finitude. It is discussed that some rather unsettling psychological consequences stem from the awareness of our reality and future, and this may lead to a variety of conscious and unconscious processes of psychological defence (Arndt & Vess, 2008). In this sense, anxiety, fear of death, thinking about the future and other general questions about the meaning of life can promote existential distress. Ritualistic/religious beliefs and practices are a potential way that humans found to deal with these difficulties – just like delusions may bring meaning. These ideas may also help explaining the possible relation between excessive symbolic thinking and the emergence of schizophrenia and psychotic disorders.

Similarly, similar aspects of our highly developed symbolism that bring suffering can enable sophisticated self-awareness and complex language, allowing us to achieve great endeavours, such as science, technological innovation, art, and poetry. This rich symbolic production allows us to make sense of our reality, making plans about the future, dealing with challenging experiences and, particularly, investigating and manipulating nature and reality.

V. Final considerations

In this thesis we aimed to discuss the role of subjective effects of psychedelics in self alterations, as well as positive and negative outcomes of their experience. This is the first study to adapt and validate the Ego Dissolution Inventory to the context of a Latin America country. Given the recent growth of studies involving psychedelics, the development of an adapted and validated instrument to assess such a central aspect of the psychedelic experience is of great importance. The Brazilian version of the scale showed solid initial psychometric properties. Further validation, including establishing the predictive validity of the instrument, should be sought. Moreover, the results allowed us to understand with more complexity the ego-dissolution phenomenon, as well as the potential benefits promoted by it.

The relationship between the subjective effects of psychedelics and positive or negative outcomes due to them was also investigated, in addition to exploring the influence of these effects in the development of human self-awareness. Although psilocybin use has been made for centuries, the reports of users' subjective experiences are not often analysed scientifically by researchers. We believe that these analyses reveal important data about the mechanisms underlying the different possible outcomes that the same substance can produce in its users. The results of this study confirms central axes of the psychedelic experience, such as the presence of somatic and visual changes, connectedness and sense of being one with the world, and the effects of the environment, as well as the positive nature of the so-called mystical experiences that the substance promotes, and the importance of the phenomenon of ego dissolution to both positive and negative outcomes.

Regarding the limitations of this thesis, we highlight the sampling bias of the first article, because recruitment was predominantly from university students, which skewed the composition of the group towards white ethnicity and higher educational attainment. In addition, some cultural difficulties in the translation of the term 'ego' as well as the semantic wording of some terms may have led to conflict in the answers. Self-selection in the second and third articles is also an important limitation; due to its non-probability sampling, it can lead to biases by only considering experiences reported by users at the website. Moreover, the lack of contextual variables, including setting-specific information, is also a limitation of these articles. Finally, there are intrinsic limitations in the hypothesis article (article 4), particularly the fact that it follows a narrative approach

in a field, palaeoanthropology, in which hypothesis testing is limited. However, the review generates several empirically testable hypotheses. Future work combining different disciplines can shed light on the relationship between ritual practises and altered states of consciousness in contemporary and ancient traditional societies.

VI. References

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