PSYCHOLOGICAL EXPLORATIONS OF THE MAGIC MUSHROOM (PSILOCYBIN) EXPERIENCE, PART II: *NEUROPSYCHOLOGICAL MEASURES*

Explorações Psicológicas da Experiência com Cogumelos Mágicos (Psilocibina), Parte II: Medidas Neuropsicológicas

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ABSTRACT

Some investigations conducted with psilocybin and mushrooms of the Psilocybe genus on the human mind point to a peculiarity of these substances to promote a special state of consciousness. The present study measured the effects of dehydrated magic mushrooms on human visual processes and memory utilizing tasks in a pre- and post-test form. We observed deficits in visual working memory and these results were consistent with other, recent psilocybin studies. However this and other visual mechanisms were not affected as measured according to the functions of the Motor-Free Visual Perception Test, suggesting an important role for unconscious attentional process in working memory tasks. Participants' performances on a manual line bisection task suggested a dominant activity of the left brain hemisphere during its realization, or synchronization of brain hemisphere activity, and seem to differ from the performance of schizophrenia subjects. In conclusion, magic mushrooms showed to be a potential tool in investigation of the psychological processes and basic functional aspects of general human cognition.

KEY WORDS: Perception; Memory; Hallucinogens; Psychedelics; Psychotomimetic; Cognition.

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RESUMO

Diversos estudos apontam a particularidade dos cogumelos do gênero Psilocybe e seu princípio ativo psilocibina promoverem um estado especial de consciência. O presente estudo apresenta os efeitos de cogumelos mágicos desidratados sobre os processos de percepção visual e memória, utilizando tarefas no formato pré e pós-testes. Foi observado déficit na memória de trabalho visual após o consumo, consistente com achados de outros estudos recentes. Entretanto, outros mecanismos visuais não foram afetados, de acordo com as funções do Motor-Free Visual Perception Test, sugerindo o papel de mecanismos atencionais em tarefas de memória de trabalho. O desempenho dos participantes na tarefa de bissecção manual de linhas sugeriu dominância de atividade do hemisfério cerebral esquerdo durante a realização da tarefa após o consumo dos cogumelos, ou sincronização de atividades dos hemisférios cerebrais, diferindo de desempenhos observados em pacientes esquizofrênicos. Em conclusão, os cogumelos mágicos se mostram como uma ferramenta potencial na investigação de processos psicológicos e aspectos funcionais básicos da cognição humana em geral.
PALAVRAS-CHAVE: Percepção; Memória; Alucinógenos; Psicodélicos; Psicotomimético; Cognição.

INTRODUCTION

The genus *Psilocybe* constitutes an important group of Fungi called magic mushrooms due to their psychoactive effects. They have been widely used as entheogens by Indians of Central America and ritual use continues until today as well and as new modes of use like hedonistic (1-3). In Brazil there are some species which occur throughout the territory (4-6).

Psilocybe are rich in the compounds psilocybin and psilocin. These compounds act primarily on the serotonergic brain system, promoting a complex altered state of consciousness characterized by modifications in perception, cognition, volition, sometimes accompanied by a sense of mystical-like experiences and believed to resembled schizophrenia and psychosis (7-12).

Current knowledge demonstrates that psilocybin is capable of interfering with cognitive mechanisms (e.g., memory processing, visual perception, perception of time, language, attention, etc.) as well in brain substrates, with particular action on limbic structures, the reptilian complex and neo-cortex (12-20). Some of these studies have revealed similarities with mental and cerebral functioning usually found in schizophrenic patients. This resemblance has led some investigation on psychopharmacology since psychedelic substances discovery by modern science about one hundred years ago are now recognized as important tools in psychosis research (10, 11, 21).

Understanding what mechanisms function in the altered states of consciousness induced by psychedelics represents an important field that seeks to explain its resemblance with schizophrenia and psychosis, as well as its psychotherapeutic potential as pointed out by some contemporary research (20, 22-28).

The present study had the objective of exploring the action of the consumption of magic mushrooms on human cognition. In this second part of our study, we present the results of neuropsychological tests, with particular attention to a discussion of the Model Psychosis Paradigm for psychedelic substances.

METHOD

Volunteers

Volunteers were selected as described in Part I of the present investigation. More details about them can be obtained by consulting the first part of the study, such as the selection criteria for participation in the study. In summary, 28 people participated

as volunteers in a magic mushroom experience and were analyzed in small groups on different days. The pattern of previous psychedelic use by the participants was categorized as "light use" (n= 9), "intermediate use" (n= 4), "heavy use" (n= 8) and "no use" (n= 7), according to the number of times and types of psychedelic substances used in their life. An additional 14 people participated as the Control Group for the Motor-Free Visual Perception Task – vertical format. The ages among these participants (Control Group) were 25.9±6 years old (19-44) and the educational levels comprised university students (n= 9) and completed secondary school (n= 5). Just one participant was put in the "heavy use" category of psychedelic substances and other volunteers presented "light use" (n= 7) and "no use" (n= 6).

Magic Mushrooms (Psilocybe cubensis)

Magic mushrooms were collected in cow pastures during the rainy season in the places indicated in the first part of the study and were identified as *Psilocybe cubensis* (Earle) Singer at the Mycology Department of the Biological Sciences Center at UFPE. Collected material was prepared and stored until use in the experiments. Dosage used was 55.6 mg/Kg of dehydrated mushrooms/person's weight (equivalent to 0.35 mg/Kg or 350 μg/Kg of active psilocybin/person's weight), according to the mean concentration of active compounds found in dehydrated *Psilocybe cubensis* (0.63%) collected in Brazil (29) (see Part I for more details).

Manual Line Bisection Test

The Manual Line Bisection Test is a traditional test used to identify and define visual deficits (30). It consists of a spatial judgment in which the participant has to indicate the center of a line with a simple trace, as accurately as possible using the dominant hand, dividing the line into two halves. Normally, sane and sober people have the tendency to misplace the bisecting line to the left, due to right cerebral hemisphere dominance in this task. Therefore, the aim of this test was to compare the effects of magic mushrooms on lateralization against that of the usual state of consciousness.

The participants realized the task comfortably seated at a desk and were verbally informed about procedures. Twenty four black lines (200 mm X 1 mm), disposed horizontally on A4 paper, and were presented individually to participants. There were four different conditions with six lines each. Each condition presented numbers as distracters located to the right of the line terminus (right distracters), left distracters, at both terminals (double distracters) or without distracters (no distracter). We used numbers as distracters (3, 4, 5, 6, 7 and 9) separated 6 mm for the termini of the lines, whose function was to observe possible influences of attention on lateralization (31). We conducted the task pre- and post-test. Post-test tasks were realized 120 minutes after magic mushroom consumption. No time limits were set for task completion. To analyze the performances we measured the deviations (millimeters) made by participants in relation of the true center of the lines (zero), with the convention of using negative values for left deviations and positive values for right deviations from zero.

Visual Working Memory Task

The Visual Working Memory Task was used to identify the effects of magic mushrooms on high-level visual processing (visual working memory). The task consisted of 16 cards with two sides on A4 paper. The front side was composed of random numbers (0-9) horizontally distributed (2x5). The back side was composed of letters in alphabetical order (a-j), each letter representing a number to be memorized from the front side (Figure 1). Cards were presented individually to the participants to be memorized. There were two different time conditions for memorization (15 and 5 seconds), composed of eight cards each.

All participants saw the cards in the same sequence. Participants were comfortably seated for this task and, after hearing the instructions, given the battery of memorizations beginning with fifteen seconds of time observation, followed by the battery of five second observations. At the end of the memorization time, the cards were immediately turned back vertically and three numbers were sorted to be indicated by the participants as the letters referred to by these numbers. Answers were noted on a response-card in number-letter format (e.g., 3-f; 9-d). Means were composed of the number of right answers and any answers without this alpha-numeric relation were considered errors. The task was conducted in a pre- and post-test format and all participants received previous training for this task. The post-test was realized 210 minutes after magic mushroom consumption. The same groups of cards were used in pre- and post-tests as well the order of memorization time (first 15 s, then 5 s), but the sequence of cards used in the batteries were inverted for the conditions of time of memorization in the post-test.

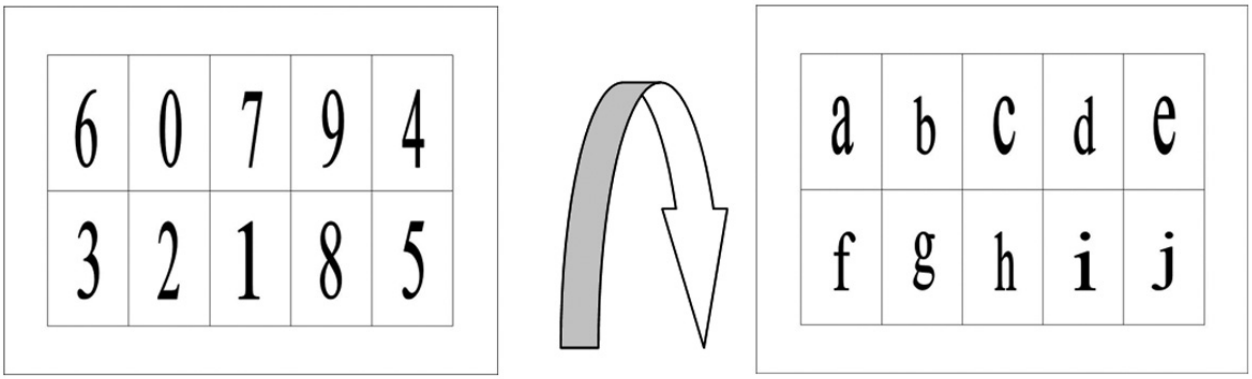

Figure 1. Example of memorization card. Each number on the front side is represented by a letter on the back side (e.g. 6-a, 8-i). The cards were vertically turned over at the end of the time of memorization. For each card, three numbers were sorted to verify the participants' visual working memory and noted in a response-card in an alpha-numeric answer format.

Motor-Free Visual Perception Test – Vertical Format (MVPT-V)

The Motor-Free Visual Perception Test – Vertical Format was applied to verify general aspects of visual perception. This test is used in psychiatry and neurocognitive explorations for visual-perceptual functions, mainly in patients with cerebral accidents and schizophrenia. It measures the following functions of visual perception: (i) visual discrimination, (ii) spatial relationships, (iii) figure-ground processing (an ability to distinguish an object from its background), (iv) visual memory, (v) visual closure (an ability to identify or complete fragments of presented pictures) and (vi) spatial relationships/figure-ground processing (31, 32). The MVPT-V permits access to the functionality of visual aspects of low-level processing (i, ii, iii and vi) and high-level processing (iv and v) according to an electrophysiological point of view. The test was applied to participants 150 minutes after magic mushroom consumption and in a control group (n=14) recruited specially for this task only (these in the usual state of consciousness). Answers were registered on

response-cards and means were based on the number of errors.

Experimental Design

The design of this study was described in Part I of this series of articles. In summary, the study was conducted in a researcher-group format in a semi-manipulated setting designed to mimic the context of recreational use of magic mushrooms. Participants came to the locale the night before of the experiment day to practice the tests and become familiar with the setting, each other and the researcher. Experiments generally began at 10 AM of the next day after completing the pre-tests of the tasks. The mental experience of magic mushrooms lasted six hours and in the fifth hour the researcher began to prepare a lunch, promoting interaction and contextualizing the end of the experiment. The group retired together between 7h 30min-8h after consumption of the mushrooms (normally between 6 and 7 PM). Participants were informed before the experiment to desist of the research at any moment if they wish, but no one did.

In the choice of the setting, we considered the role of diminishing/avoiding any incidence of anxiety as well avoiding any laboratorial contextualization of the experience by the participants. The setting successfully mimicked an original context of recreational use and participants presented excellent performance and motivation to be integrated in the research. The efficacy of the successful setting points to the importance of environmental design on the psychedelic experience. The power of intervention by external factors is not clear but has been demonstrated in other experiments (33-35).

No placebo procedure was adopted in this study due to questions referring to sample size, fragility of the placebo when applied to groups and in order to maintain group unity in the same state of consciousness as well to obtain more data. It was understood that conducting the experiment in the proposed format would impact the quality and quantity of data and the control of anxiety in participants, if controls other than pre- and post-tests, like double-blind or blind procedures, were employed. Another reason was that any placebo would be quickly discovered and might emotionally alter the experience of the other participants, as shown in previous studies with a similar format (9, 36).

RESULTS

Manual Line Bisection Test

To verify the differences of means obtained in this task (n= 28) an analysis of variance with repeated measures was realized considering as variables within-subject Test Phase (2: pre-test and post-test) and Type of Distracters (4: no distracter, right distracter, left distracter, double distracters). A highly significant main effect was found just for the Type of Distracter [$F(3, 81)= 46.472$; $p<0.001$]. The main effect of the Test Phase and its interaction with the Type of Distracter was not significant. No significant differences were found in the values obtained for the Test Phase when compared to categories of psychedelic substance use of the participants.

A posteriori Tukey analyses showed that means for right distracter and left distracter were statistically different between them (difference = 3.80 mm; $p < 0.001$) and between the other types of distracters [(right distracter – double distracter, difference = -1.76 mm; $p < 0.001$); (left distracter – double distracter, difference = 2.04 mm; $p < 0.001$); (right distracter – no distracter, difference = 1.66 mm; $p < 0.001$); (left distracter – no distracter, difference = -2.13 mm; $p < 0.001$)]. No statistically significant differences were found between Double Distracter and No Distracter (difference = -0.09 mm; $p = 0.816$). The results show the influence of the right and left distracters on visual lateralization, with more prominent influences of left distracters in promoting deviations from the true center of the lines.

We observed that participants were more accurate in the divisions of the lines at conditions of No Distracters and Double Distracters in the post-test, however with higher standard deviations. Results in the pre-test had higher tendencies toward left deviations for all types of distracter conditions, except for right distracter, indicating activity dominance of the right cerebral hemisphere. After magic mushroom consumption, we observed a contrary effect with tendencies to right lateralization, except under the condition of right distracter, indicating an increase in activity dominance of the left cerebral hemisphere in the post-test than in pre-test.

Therefore, we verified the differences between values obtained under distracter conditions in relation to the true center (zero) of the lines. The means between the distracter conditions and Phase Test (pre- and post-test) were compared by the paired Student-t test. Participants had higher accuracy in the post-test for the conditions of Double Distracters and No Distracters as means for these were not statistically different from zero, as opposed to the observed means in the pre-test [double distracter (pre-test, t = -2.40; p = 0.024; sd = 3.53); (post-test, t = -0.85; p = 0.401; sd = 4.43)]; [no distracter (pre-test, t = -2.59; p = 0.015; sd = 3.39); (post-test, t = -0.55; p = 0.583; sd = 4.45)]. The values obtained for left distracters were always different from zero in both phase tests [pre-test (t = -5.00; $p < 0.001$; sd = 3.35); post-test (t = -3.79; $p < 0.001$; sd = 4.51)], however means for right distracters were always statistically equal to zero [pre-test (t = 0.28; p = 0.778; sd = 3.48); post-test (t = 1.16; p = 0.257; sd = 4.63)]. Figure 2 summarize the results found.

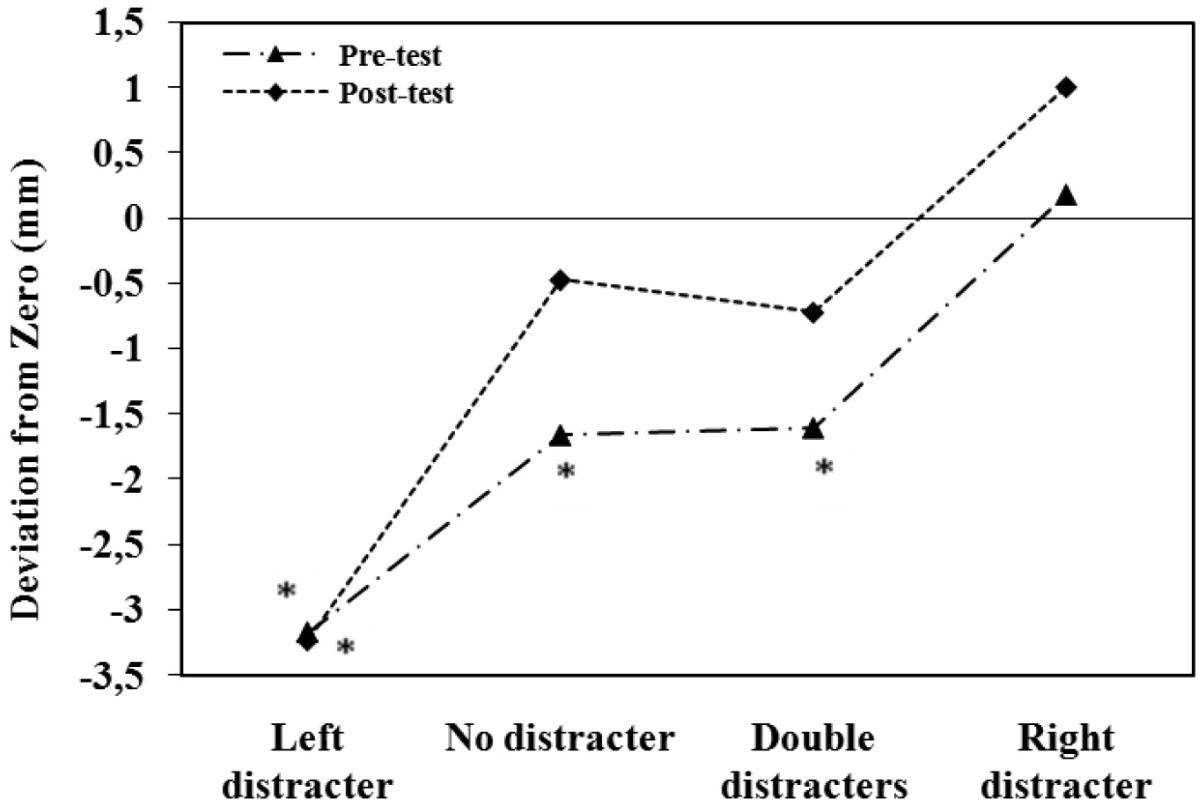

Figure 2. Results of the manual line bisection task obtained before and after magic mushroom consumption. Participants presented in the post-test a tendency to realize right lateralization, though this was not significant statistically. The * indicates statistically significant differences between means and the true center of the lines (zero) ($p < 0.05$).

Visual Working Memory Task

We investigated the difference between means of participants' right answers obtained in this task through variance analyses of repeated measures considering as within subject variables the Test Phase (2: Pre-test and Post-test) and Memorization Time (2: 15 and 5 seconds). We found a strongly statistically significant effect just for the Test Phase [$F(1, 27) = 17.782$; $p < 0.001$]. The mean effect for Memorization Time was not statistically significant. *A posteriori* Tukey analyses verified differences of means obtained in memorization under both time conditions (15 and 5 seconds), indicating high memorization rates in the pre-test phase {difference pre-/post-tests [$(15/15) = 0.38$; $p < 0.001$]; [$(5/5) = 0.21$; $p < 0.02$]}. No statistical differences were found in memorization rates considering categories of psychedelic use of the participants. Results are summarized in Figure 3.

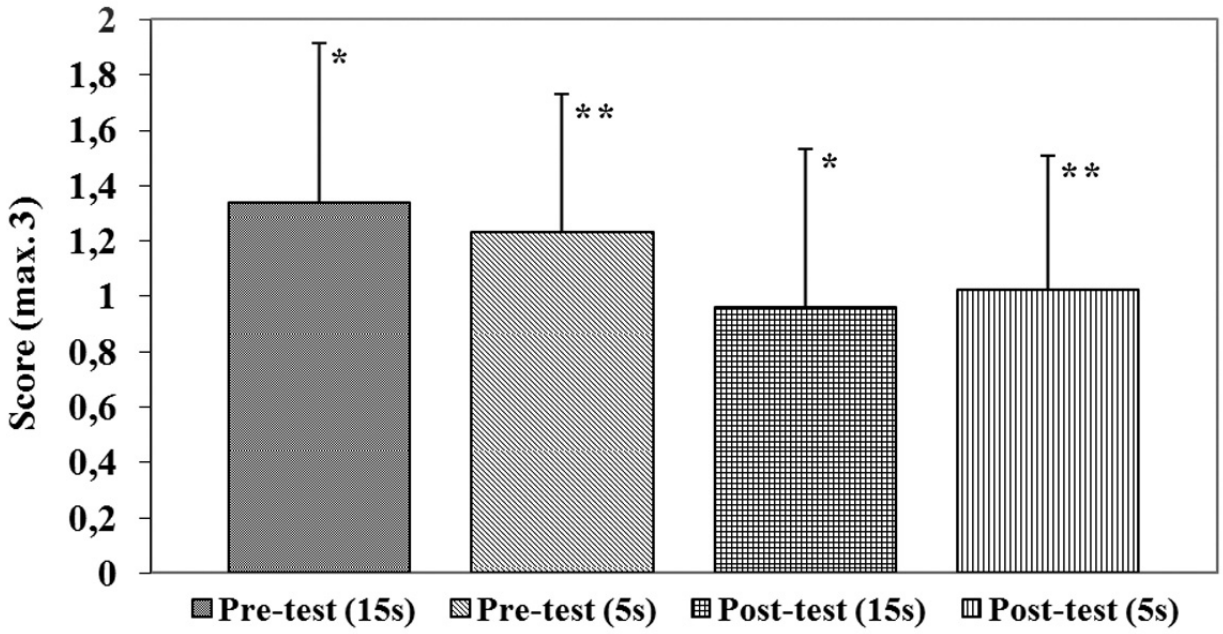

Figure 3. Mean rates obtained by participants in the visual working memory task in the pre- and post-tests. Only the test phase was statistically significant (* $p < 0.001$; ** $p < 0.02$).

Motor-Free Visual Perception Test – Vertical Format (MVPT-V)

This task was applied to the participants of the study only under the magic mushroom state of consciousness (n = 28) and in a Control Group (n = 14), under the ordinary state of consciousness. The differences between means were verified by variance analyses of repeated measures considering within subject variables the MVPT-V Functions (6: visual discrimination, figure-ground, visual memory, visual closure, spatial relationships and spatial relationships/figure-ground) and categories of psychedelic substance use (4: no use, light use, intermediate use and heavy use). We found a statistically significant mean effect just for MVPT-V Functions ($F(5, 120) = 3.425$; $p < 0.01$), indicating the sensitivity of the task in measuring different visual functions. No statistically significant differences were found in global means of MVPT-V functions obtained by participants compared

to that means of the control group, according to One-Way ANOVA, indicating that mushrooms do not affected in an important way the general functions of visual perception (Table 1).

TABLE 1. Means of errors and standard deviations obtained by participants and the control group in the different visual functions measured by the Motor-Free Visual Perception Test (a= 0,05).

MVPT-V Visual Functions	Participants	Control Group	*P*
Visual Discrimination	0	0.71±0.27	0.16
Figure-Ground Processing	0.14±0.36	0.21±0.58	0.62
Visual Memory	0.50±1	0.71±1.14	0.54
Visual Closure	0.64±1.06	0.43±1.09	0.54
Spatial Relationships	0.25±0.7	0.14±0.36	0.60
Spatial Relationships/Figure-Ground	0.14±0.36	0.07±0.27	0.51

DISCUSSION

In the previous study (Part I of this study) we showed that values obtained in the HRS-test were similar to those found in a psilocybin study (28), indicating a median-high psychedelic experience. Participants were ordered according to the pattern of variety and quantity of psychedelic substance use (see Part I, Table 1). As pointed out by some authors, psychedelic substances may be important in investigations of the biological model of psychosis and schizophrenia (11-13, 18, 37-40). Therefore, here we aimed to compare deficiencies normally presented by people with mental illness on memory and visual perception, as a way of defining similar peculiarities of altered states of consciousness caused by magic mushrooms and their psychotomimetic characteristics on these variables.

We observed significant deficiencies in the visual working memory task after magic mushroom consumption, revealed as decreased memorization rates compared to the pre-test. These results are in line with a previous psilocybin study investigating spatial working memory (19), however other cognitive mechanisms could explain these alterations, e.g. attention, as was seen in another psilocybin study that failed to find deficiencies in working memory (15). We did not find deficiencies in short-term working memory as demonstrated in a more specific task, the MVPT-V test. We believe that attention could be more affected than working memory in the psychedelic experience, explained according to Ornstein's Theory, in which a maximum limit of information processing causes deficiencies in memory and attention (41). Considering that psychedelics can "break" the natural filtering of information, the thalamus, some internal and external intrusive information reaches the neocortex, causing overload of information processing (12, 18), in this way, attention and memory are affected by exceeding the brain's capacity to save data for short periods.

Content storage limitations have been found in the brain system under normal, everyday circumstances (42). This means that an increase of information processing in the brain can result in anomalous functioning of memory and attention can also be affected once you have an overload of stimulation (from perceptual and affective sources). The following example of a participant's discourse shows the effects of exaggerated intrusive information: "It's too much information at the same time, everything at the same time."

The visual working memory function measured by MVPT-V was not affected in the participants, neither were the other MVPT functions. This was not an expected result since statistical differences have been found in another visual working memory task and because of the belief that psychotomimetic characteristics of altered states of consciousness caused by magic mushrooms could be similar to the results for MVPT-V found in schizophrenic and depressed patients (31). Psilocybin has been demonstrated to act on high-level brain processing (17, 19); schizophrenia and depression also cause deficiencies in some low- and high-level visual processing (31). However, the psychotomimetic experience caused by magic mushrooms did not affect visual functions of the MVPT-V task, suggesting a difference between the psychedelic consciousness state and the schizophrenic states.

A possible explanation for this could be related to the type of task applied to investigate psilocybin action on memory. Schizophrenia subjects have presented deficiencies in the focal attentional mechanism in comparison to healthy people (43, 44). Results of the memory tasks applied to investigate memory deficiencies provoked by psilocybin and magic mushrooms do not show a clear role of attentional processes in its construction. Here, we believe too that our deficiency results in visual working memory test could be mixed with deficiencies in attentional mechanisms. For us, it was impossible to define how much interference this had on visual working memory, as we did not include any attentional process control. Further research is necessary to focusing on attention, in construction of methods trying to isolate its effects in general human activity, looking for its peculiarities in ordinary mental experience and altered states (45).

Participants presented a significant tendency in the lateralization realized on manual line bisection test according to the type of distracters. In the pre-test, participants showed the natural leftward lateralization observed in normal subjects, statistically significant in relation to the true center of the lines in the task. This phenomenon is known as pseudo-neglect and reflects the dominance of right brain hemisphere activity required in the realization of this task, in which healthy humans present a natural tendency to neglect the right hemispace (31, 46-49). Our results showed that the performance of participants after magic mushroom consumption presented a tendency to realize rightward lateralization, in which we observed approximations of the values with the true center of the lines. That is, participants did more accurate bisections in the post-test, neglecting the left hemispace, a pattern different from that observed in schizophrenic patients (31, 50).

In the task of manual line bisection, schizophrenic patients showed significant tendencies to realize exaggerated left lateralization compared to healthy people. Some authors have discussed if these results could represent a lateralized anomaly of attentional levels or the possibility of its existence in a representational level in schizophrenics (31, 50, 51). The hemi-neglect phenomenon in schizophrenia is defined as a failure to present a stimulus response in a determined hemispace, a failure observed in patients with parietal lesions (48, 49, 52). These hemi-neglected deficiencies observed in schizophrenia could reveal important deficiencies in visual-perceptual, high-level processing (53, 54).

Our results of the differences of the participants' performances from that presented by schizophrenic patients on the manual line bisection task can indicate an imbalance of brain hemisphere activity dominance, suggesting tendencies in the participants under the psychedelic state of consciousness to consider right hemispace and neglect left hemispace, explaining the accuracy of the marks in the middle of the lines. It is important to remember that these results were not significant in relation to the phase test, but it was significant in relation to distracter conditions. That is, after magic mushroom consumption, the participants were more influenced by right distracter conditions and right hemispace, neglecting the left hemispace and showing, according to the manual line bisection task paradigm, prevalence or increase in the activity of the left brain hemisphere.

Some studies have pointed to an increase in the activity dominance of the right brain hemisphere

in schizophrenia, a condition totally different from our observations (31, 48-51). This leads us to consider the resemblance of psychedelic states and psychosis, suggesting limitations and caution in these comparisons. Our results do not reflect the right hemisphere dominance shown in neuro-imaging studies of psilocybin action on the brain (18). However, another neuro-imaging study with psilocybin showed a tendency toward symmetry of brain hemisphere activity (13), a finding of brain behavior more related to our results.

We think it is important to pay attention to idiosyncrasies and uncertainties in the patterns of brain activity during task realizations under the psychedelic state of consciousness (13, 14). Maybe, performance on the manual line bisection test of the participants of our study could be different from schizophrenic patients because the magic mushroom mental experience resembles acute states of schizophrenia (11, 12, 55), and performances on the manual line bisection test of schizophrenic patients were related to chronic schizophrenia (50).

In conclusion, magic mushrooms have high potential as a tool in the investigation of the Model Psychosis Paradigm for psychedelic substances. We observed deficiencies in working memory, in which we reflected about the real importance and interference of attentional mechanisms in the performances made by participants, previously demonstrated in psilocybin studies and in conformity to psychosis. We found evidence for a preference of the participants to be more attentive to data in the right hemispace in the altered state of consciousness, suggesting high activity to the left brain hemisphere, a behavior different from that previously observed in schizophrenics. The absence of interference of the magic mushroom experience on low processing functions of visual perception was demonstrated at the dosage applied in the present study. We cannot find any statistically significant differences in the tasks used, neither by relating to categories of psychedelic substance use, groups of participants nor gender at our sample size. We believe that some neuro-functional studies are still required to establish the patterns of brain activity for specific cognitive tasks under altered states of consciousness caused by psychedelics in order to understand their influences on brain activity behavior.

Finally, psychedelic consciousness states seem to have some similarities with psychosis and schizophrenia, mainly when phenomenological aspects are considered, but it is important to understand the manifestations of these similar cognitive characteristics and their relationships with entheogenic use of psychedelic substances. If psychedelic states are related to psychopathology, perhaps they can offer high psychotherapeutic potential (7, 8, 20, 34, 56-62)? The current perspective of psychedelic research can lead us to new and important discoveries in human cognition and consciousness functioning. The follow-up investigation of the participants in the present study can reveal relevant aspects of the experience for their lives as well as suggest new directions of research.

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