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ORIGINAL INVESTIGATION

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Effects of ayahuasca on binocular rivalry with dichoptic stimulus alternation

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Abstract *Rationale:* During binocular rivalry, two incompatible images are presented to each eye and these monocular stimuli compete for perceptual dominance, with one pattern temporarily suppressed from awareness. One variant of stimulus presentation in binocular rivalry experiments is dichoptic stimulus alternation (DSA), when stimuli are applied to the eyes in rapid reversals. There is preliminary report that in contrast with healthy controls, schizophrenic patients can maintain binocular rivalry even at very high DSA rates. *Objective:* The study was undertaken to investigate whether binocular rivalry survives high rates of DSA induced by the South American hallucinogenic beverage ayahuasca. *Methods:* Ten individuals who were participating in ayahuasca ceremonials were requested to volunteer for binocular rivalry tests (DSA=0, 3.75, 7.5, 15 and 30 Hz) without and after drinking the brew. *Results:* Ingestion of ayahuasca increased mean dominance periods both in standard binocular rivalry conditions (no DSA) and tests with DSA. At higher DSA rates (15 and 30 Hz) the total length of dominance periods was longer on the brew. *Conclusion:* It is discussed that ayahuasca-induced survival of binocular rivalry at high DSA rates may be related to slow visual processing and increased mean dominance periods may result from hallucinogen-induced alteration of gamma oscillations in the visual pathways.

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Introduction

Binocular rivalry belongs to a class of visual illusions in which an ambiguous but unchanging sensory input leads to sudden perceptual switches (Blake 2001). Rivalry occurs when dissimilar images stimulate corresponding retinal areas of the two eyes. For example, if a grating of horizontal lines is presented to the right eye while a grating of vertical lines is presented to the left, the usual experience is of quasi-regular, but unpredictable switches between two perceptions: for 1 s or more, the majority of subjects see only horizontal lines and then for 1 s or more, only vertical lines in an alternating manner (Pettigrew and Miller 1998). Despite the fact that both images are continuously presented during rivalry, the image of one eye disappears from awareness (i.e. suppressed), while the other eye's image is seen (i.e. dominant). Although the phenomenon has been known from the 19th century, lately there has been a resurgence of interest in studying binocular rivalry due to its quantifiable characteristics and new evidence about its neural locus and mechanism.

Several theories have been proposed to account for binocular rivalry (Blake 1989; Fox 1991; Miller et al. 2000; Blake and Logothetis 2002). Such theories generally suggest that because increased thresholds occur during periods of rivalry suppression, the suppression originates from some type of cortical inhibition. Specifically, binocular rivalry was proposed to result from reciprocal inhibition of monocular neurons in the primary visual cortex (Blake 1989). In contrast to the early bottom-up concept, Sheinberg and Logothetis (1997) have demonstrated that activity in higher structures of the visual pathways, such as the inferior temporal cortex and the superior temporal sulcus, correlates better with the visual percept than the activity in the primary visual cortex. Referring to their findings, Dayan (1998) argues that perceptual alternation can be generated by competi-

tion between top-down cortical interpretations for the disparate inputs. Some mapping studies maintain that primary visual cortex is the site of rivalry (Polonsky et al. 2000; Tong 2003), although the possibility has not been excluded that these results could be the consequence of top-down influences from higher levels. The present consensus is that rivalry is a multi-level process that reflects low-level sensory processing as well as high-level cortical activity (Blake and Logothetis 2002).

One variant of stimulus presentation in binocular rivalry experiments is dichoptic stimulus alternation (DSA). In studies using DSA, stimuli are applied to the eyes in rapid alterations instead of keeping the stimulus presented to each eye constant, as in the classical paradigm (Logothetis et al. 1996). DSA at frequencies much higher than the natural frequency of binocular rivalry can unveil underlying deficits in visual neural transitions. This modified method revealed that, in contrast with comparison subjects, schizophrenic patients could maintain slow perceptual alternations even with very high DSA rates (Frecska et al. 2003; Wright et al. 2003). The survival of binocular rivalry at high DSA rates in schizophrenia may reflect impairment in visual information processing and result from loss of presented stimuli when the visual cortex is not capable of following high rates of stimulus change. Slow visual information processing has been repeatedly demonstrated in schizophrenic patients (for review, see McClure 2001). In schizophrenia, visual targets require a longer processing time to "escape" the effects of a subsequent stimulus (Braff and Saccuzzo 1982; Saccuzzo and Braff 1986; Weiner et al. 1990; Rund 1993; Butler et al. 1996). At high DSA rates, there is insufficient time available in schizophrenic patients for extended processing and the resulting under-sampling maintains binocular rivalry, despite the increased frequency (Frecska et al. 2003).

There is evidence that abnormalities in 5-HT_{2A} receptor dependent neurotransmission play a role in some symptoms and perceptual-cognitive deficits in schizophrenia. Some of this evidence comes from the observation that indoleamine hallucinogens can induce 5-HT_{2A} receptor-mediated (Aghajanian and Marek 1999) symptoms that resemble symptoms of schizophrenia (Vollenweider et al. 1998). Dysfunctional 5-HT_{2A} receptors may be involved in abnormal sensory gating mechanisms in schizophrenia (Geyer 1998). Furthermore, the 5-HT_{2A} antagonist property shared by atypical antipsychotic medications may play a role in their ameliorative effects on schizophrenic symptoms not affected by classical D_2 receptor-blocking agents (Meltzer and McGurk 1999; Umbricht et al. 1999; Purdon et al. 2000).

N,N-Dimethyltryptamine (DMT) is the active indoleamine ingredient of ayahuasca which is a hallucinogenic decoction made of psychoactive plants (*Banisteriopsis caapi* and *Psychotria viridis* or *Diplopterys cabrerana*) indigenous to the Amazon and Orinoco river basin of South America. Known under different names such as yagé, natem, mihi, dapa, kamarampi and many others, the brew has been used, probably for millennia, for medico-religious purposes by numerous indigenous groups of the Upper Amazon (Dobkin de Rios 1972; Schultes 1982; Luna 1984, 1986). The ritual use of ayahuasca has spread among Amazonian mestizo population of Colombia, Ecuador, Peru and Brazil. In Brazil, its use has taken a new course as members of synchretic Christian religious organizations, with strong Afro and Amerindian influences, have adopted it as a sacrament under the names of Santo Daime and Hoasca. Although its use is tolerated in countries sharing the Amazon basin, Brazil is the only country where it currently enjoys legalized status. Its active ingredients are the reversible monoamine oxidase inhibitor harmine and harmaline, the serotonin-reuptake inhibitor tetrahydroharmine, which makes the 5-HT_{2A} agonist component DMT bioavailable for oral use, relatively potent and long-acting (Callaway et al. 1999). In this combination, DMT is capable of eliciting a condition characterized by vivid visual imagery, auditory hallucinations, cognitive changes, and depersonalization-derealization type phenomena with profound modification in the sense of self and reality (Szara 1956; Strassman 1996; Riba et al. 2001). The typical onset of action is within 60 min and the peak of effect is between 90 and 120 min after drinking the brew (Riba et al. 2003).

The purpose of present study was to investigate whether binocular rivalry could illuminate common mechanisms in schizophrenia and 5-HT_{2A} mediated hallucinosis induced by ayahuasca. In line with previous findings in schizophrenic patients, we postulate that ayahuasca ingestion will induce a similar condition: the continued presence of binocular rivalry at high DSA rates.

Materials and methods

Subjects

Data were obtained from ten individuals who were participating in ayahuasca ceremonials held in Florianópolis, Brazil between April 1 and 29, 2002 and were volunteering for the binocular rivalry tests. The site in Brazil was chosen for the reason that consumption of ayahuasca is legalized in that country. Enrolled volunteers ingested the decoctum for ritualistic purposes and not for participation in the study. The Principal Investigator (L.E.L.) obtained written informed consent from participants for the binocular rivalry tests prior to the ingestion of the psychoactive brew, conforming to the guidelines set forth by the Ethical Principles and Guidelines for the Protection of Human Subjects of Research (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research 1979). Originally, 15 candidates were considered for participation. One of them was not eligible because she had a dose below the range set in the inclusion criteria. Two individuals did not participate because they preferred not to be disturbed during the sessions, one of them had mixed handedness, and one male was excluded due to cannabis dependence. The final experimental group included eight males and two females with a mean age of 52 (SD=8.8; range=34–65) years and a mean weight of 71.8 (SD=11.4; range=48–82) kg.

Inclusion criteria for experimental subjects were: 1) being experienced in ayahuasca use (having at least five previous sessions); 2) ingesting ayahuasca in a dose not less than 50 ml at the beginning of the experimental session; 3) right handedness, which was evaluated with a modified Edinburgh questionnaire

(Briggs and Nebes 1975); 4) a likelihood ratio (hits/false alarms) at least 3-fold better than random guessing in a signal detection task designed to mimic the perceptual switches of binocular rivalry (see below).

Exclusion criteria for experimental subjects were: 1) personal history of psychiatric or neurological disorder and/or use of psychotropic medication for non-psychiatric condition (e.g. anti-depressant for chronic pain, psychostimulant for weight loss); 2) head injury leading to loss of consciousness for greater than 5 min; 3) alcohol, or illicit drug use in the past 3 weeks; 4) lifetime history of substance dependence as diagnosed by DSM-IV (American Psychiatric Association 1994); 5) body mass index <20 or >25 kg/m^2; 6) having history of cardiac, endocrine illness; 7) nausea with vomiting before the rivalry test was completed; 8) lack or mild degree of ayahuasca experience during the experimental session (see below).

A further sample of 110 undergraduate college students provided control data on binocular rivalry under conditions of DSA that served to verify in a non-age-matched population the very low incidence of perceptual alternation at high rates of DSA in the normal population. Test-retest validation of the quantitative measures of binocular rivalry was performed in 32 subjects.

Ayahuasca session

Participants maintained a salt, sugar and alcohol free diet for 4 weeks during their partaking in the seminar organized by the Wasiwaska Center, had three to four sessions per week, and were enrolled into the rivalry study during week 4. The provided traditional diet did not include fermented or smoked food, aged/dried/cured meat products, and beverages known to have high tyramine content. On the test day, subjects avoided solid food for 12 h starting from 1:30 p.m. At 7:30 p.m. they ingested a self-chosen dose of ayahuasca (obtained from one of the Brazilian synchretic churches) ranging from 50 to 100 (mean=74, SD=21.2) ml. The alkaloid concentrations of the beverage were analyzed later with the method of Callaway et al. (1996) and were as follows: harmine 1.36 mg/ml, tetrahydroharmine 1.05 mg/ml, and DMT 0.73 mg/ml. For the following 4 h, subjects rested supine with lights turned off. Volunteers performed the rivalry test between 90 and 150 min after the ingestion of ayahuasca and had the test done on a separate day in the evening hours without the influence of the decoction (baseline comparison). Six of them had binocular rivalry with ayahuasca as the first procedure and four were scheduled to have the test first without having the brew. Based on participants' previous experiences, the global subjective experience induced by the brew was rated on a 5-point Lickert scale ranging from 0 to 4 (none, mild, moderate, strong, very strong) immediately before starting the binocular rivalry test.

Rivalry procedure

The technique for eliciting binocular rivalry was similar to that already published, with two small targets presented foveally so that the right eye saw, for example, a horizontal grating and the left eye saw a vertical grating, in the same apparent location (Pettigrew and Miller 1998).

Display apparatus

Custom software (written by K.D.W.) generated the rivalry stimuli in frame or field sequential formats, measured responses, and provided user interfaces. In the frame sequential format, odd numbered frames were presented to one eye while even numbered frames were presented to the other eye. The software was triggered by the video vertical synch, which caused the next stimulus to be displayed, then read and stored the status of mouse buttons, and waited for the next vertical synch. Three experimental subjects wore a head-mounted display (Virtual I-O iGlasses) with SVHS resolution, which was synchronized to the frames generated by an IBM Thinkpad computer using 1024×768×256 at 75 Hz non-interlaced graphics (N-mode) by an AverMedia Averkey SVHS scan converter. The iGlasses 3D head-mounted display has separately driven LCD displays (180,000 pixels) for each eye, giving resolutions of 225×266. The other seven experimental subjects wore VRex VR Visualizer LCD shutter glasses, which alternately excluded odd or even fields presented on a 1024×768 resolution 14-inch video monitor. In the latter case, the graphics mode was interlaced at 87 Hz (I-mode). Control subjects wore VRex VR Surfer LCD shutter glasses and viewed 17 inch video monitors on which the 1024×768 display was interlaced at 96 Hz (U-mode).

Stimuli

The stimuli consisted of white binocular fixation guides centered within which was a 1° disk filled with horizontal or vertical grating. These fixation guides consisted of 1) a rectangular frame drawn around the borders of the 12×9° screen, 2) a circle 9° in diameter centered on the screen center, and 3) a plus-sign shaped crosshair at the screen center for which the centermost 3° horizontal and vertical were removed. All stroke widths for the fixation guides were about 1/16° wide. The 1° disk at the screen center was filled with 5 cycles per degree square wave gratings oriented horizontally or vertically. The disk could be presented binocularly (same grating orientation in both eyes) or dichoptically (different grating orientations in the two eyes).

Training in the reporting task

Subjects were trained how to use a two-button computer mouse to indicate what kind of gratings they perceived. In this task they were presented with binocular stimuli (both eyes received the same stimulus, there was no rivalry) while holding the computer mouse in both hands (with left thumb above the left button, right thumb above the right button). These binocular stimuli looked exactly like the experimental stimuli (save that the experimental stimuli used dichoptically presented disks). When the grating was horizontal, subjects were instructed to push, and held down the left button. The left button on the mouse had three black horizontal stripes made of plastic tape in order to be tactually distinctive for the left thumb and to provide tactile cue as reminder. The subjects were advised to move their thumb along and across the stripes to feel this cue for the horizontal report button. They were also told to keep this button held down for the entire time they saw horizontal lines in the disk. The right mouse button had three black plastic tape stripes attached vertically to it.

When subjects saw vertical lines filling the disk, they were supposed to hold down the right button for as long as they saw vertical lines and were reminded to move their thumb along and across the stripes to feel this shape cue. When the disk was filled with superimposed horizontal and vertical lines (a plaid or crosshatch), the subject was told to report this appearance by holding down both mouse buttons. Lastly, in case the disk was filled with a homogeneous field (blank) the subject was instructed to let up both buttons, and, when unsure what to report, to press nothing.

Signal detection analysis of reporting accuracy

This task was run with a computer generated video sequence that simulated rivalry alternation using binocular stimuli. Stimulus durations were sampled at equal probability intervals from a cumulative gamma distribution (Levelt 1965), and the disk content (horizontal, vertical, plaid, blank) randomly assigned that duration, with the proviso that two durations with the same content could not occur in immediate succession. A 90 s sequence of such quasi-randomly selected stimuli changed unpredictably in pattern content

and duration, but in such a way that 25% of the time each pattern appeared. A software program scored the observer's button presses during the video presentation. Responses were scored correct or incorrect by the software depending upon which stimulus pattern preceded pressing of the button(s). These calculations were carried out for time lags between stimulus and response from 0.3 to 3.0 s in 0.1-s steps, comparing button press to stimulus each 1/60 s. Random guessing produces 25% correct (hits) and 75% wrong (false alarm) choices. An observer was not allowed to begin the experiment unless three of the four response types reached a criterion of least 50% hits. The computer video could be repeated if further training was found to be necessary. Repetition did not have to be done more than once with participants of this study. The training and evaluation procedures were generally be completed in about 5 min. Typical performances were 85–95% hits with 5–15% false alarms, by observers without the drug and 70–90% hits with 10–30% false alarms by the same observers under drug influence. Estimated response latency (time lag for maximum percent correct) was 0.65 s without ayahuasca and 0.93 s on ayahuasca. No observer had to be excluded from further participation due to failure to achieve criterion performance (3 times greater likelihood of correct:wrong responses than random chance).

Experimental sequence

We presented standard binocular rivalry for 6 min (in multiple epochs) to obtain the endogenous perceptual alternation rate, and presented dichoptic reversal stimuli at 3.75, 7.5, 15, and 30 reversals per second in four 1.5-min epochs. Order of presentation of standard rivalry and the four reversal rates was counterbalanced within subject. At the end of each epoch, a graph of the responses was displayed. The experimenter described in words the general features shown in the graph in order to verify that these recorded responses were representative of the subject's perceptions. The experimental procedure was completed in 20–30 min.

Data management

For the purpose of identification, all subjects received an alias upon entering the study to aid in maintaining confidentiality. For binocular rivalry, the raw data consisted of the time (in one video frame increments) each button press lasted. These data were imported into spreadsheets and analyzed with macros that extracted the lengths of time when horizontal, vertical, plaid responses or nothing was reported. The following quantitative measures were used to characterize performance for binocular rivalry: 1) "mean dominance period" (MDP)=total duration of horizontal and vertical responses in seconds divided by the number of horizontal and vertical responses; 2) "percentage of dominance periods" (PDP)=% of total time reporting horizontal or vertical responses. Since 0.5 s is close to the mean reaction time during the video simulation sessions, button presses lasting less than 0.5 s were excluded in the analyses, as being too short to be perceptually meaningful. Data were analyzed by Student *t*-test for paired samples and by repeated measures ANOVA (Statistica for Windows v6.0) for multiple variables.

Results

All subjects, regardless of drug condition (with or without ayahuasca), showed binocular rivalry with traditional stimulus presentation (DSA=0 Hz). They reported successive percepts of a horizontal grating or a vertical grating (dominance periods) and sometimes a blend of horizontal and vertical gratings mixed with uncertain responses (non-dominance periods). The typical pattern of perceptual alternation is illustrated for one participant without ayahuasca in Fig. 1. Periods of horizontal dominance appear as blocks below the time line, periods of vertical dominance as blocks above the line, and periods of the blended (plaid) or uncertain percepts as blocks straddling the line.

Analysis of standard rivalry epochs

Our sample of 32 comparison subjects indicates that MDP is stable characteristic within an individual over periods of days or weeks (MDP test-retest r=0.69). Ayahuasca increased MDPs: mean±SD of MDP (no-brew versus on-brew)=2.9±1.5 versus 4.4±0.9, t=–2.29, P<0.05. Our subjects did not respond significantly longer to the video simulation of binocular rivalry (see "Signal detection analysis of reporting accuracy" in Materials and methods) on brew than with no brew (paired t=1.62, NS). Therefore, the longer MDPs during the ayahuasca-induced conditions cannot be explained by response perseveration. The total length of dominance periods in the four standard rivalry epochs was not different on the brew: mean±SD of PDP (no-brew versus on-brew)=86.9%±10.2 versus 79.7%±14.8, t=–1.32, NS. In comparison subjects the PDP had a test-retest value r=0.83.

Analysis of DSA epochs

When conditions of DSA were used in subjects without the brew, patterns of responding unlike those in traditional rivalry were evident. With 3.75 Hz and 7.5 Hz DSA rate, subjects reported horizontal switching with vertical at a very high rate, consistent with the flickering changing orientations presented to either eye and in an effort following the stimulus alternation (Fig. 2). Consequently, after applying the 0.5 s cut-off, less dominance period was reported as compared to the standard epochs, which were performed with constant stimulus presentation to

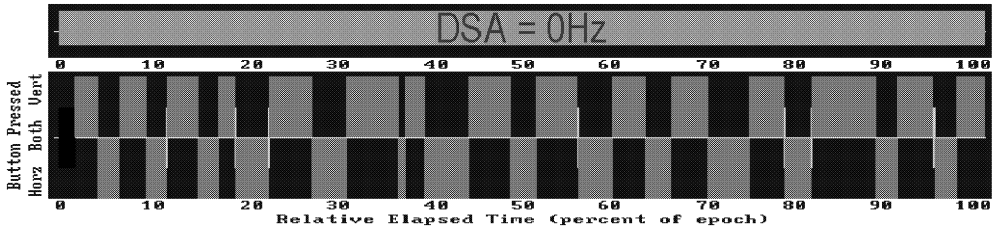

Fig. 1 Typical pattern of perceptual alternation in traditional binocular rivalry without ayahuasca

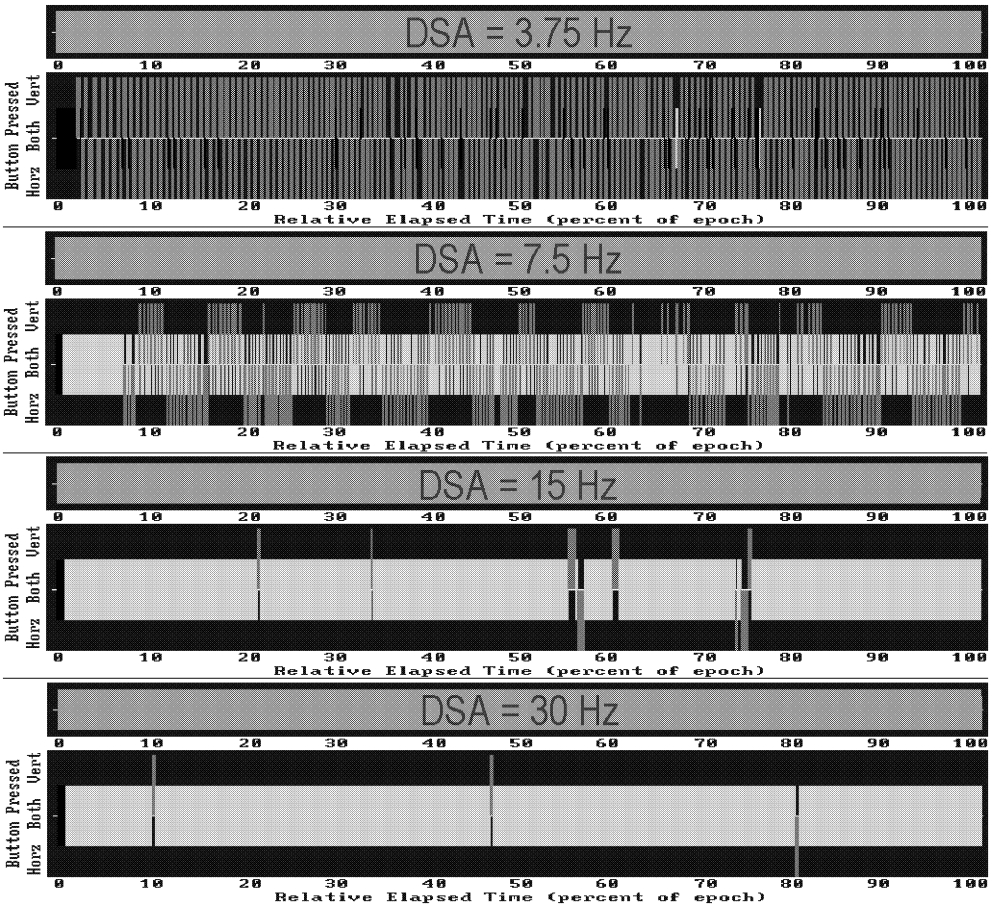

Fig. 2 Typical patterns of perceptual alternation in binocular rivalry at different DSA rates without ayahuasca

each eye. The mean±SD of PDP ($DSA_{3.75\ Hz}$ and $DSA_{7.5\ Hz}$)=24.1±26.3% and 35.1±33.9%. With 15 and 30 DSAs per second, the blended percept (crosshatch) was reported consistently, as though these even more rapidly flickering orientations had fused. Even less dominance periods were noted: mean±SD of PDP ($DSA_{15\ Hz}$ and $DSA_{30\ Hz}$)=1.6±2.3% and 4.2±7.6%. There were individual differences inasmuch as some subjects reported a few periods of horizontal or vertical dominance lasting for a few seconds, with one or more of the DSA rates. The means±SD of MDPs for 3.75 Hz, 7.5 Hz, 15 Hz and 30 Hz DSA rate were 0.9±0.6, 1.4±1.1, 0.9±1.7, and 1.3±2.5, respectively. In summary, the flicker-like response pattern or the blended percept reports were quite typical for subjects in the control condition (no brew). A similar finding was previously reported by Logothetis et al. (1996), although their study used lower DSA rates.

Under the influence of ayahuasca, subjects reverted to show typical patterns of binocular rivalry, which were more striking at the high DSA rates (Fig. 3). At low DSA rates (3.75 Hz and 7.5 Hz), the total length of the dominance periods was the same as in conditions without ayahuasca: mean±SD of PDP ($DSA_{3.75\ Hz}$ and $DSA_{7.5\ Hz}$)=39.5±26.5% and 28.9±30.1% [$F(1,9)=0.34$, NS]. As the DSA rates were increased above 7.5 Hz, the PDPs on the brew diverged from those in the control condition: mean±SD of PDP ($DSA_{15\ Hz}$ and $DSA_{30\ Hz}$) = 28.2±36.1% and 9.8±9.4% [$F(1,9)=6.5$, $P<0.05$]. The average length of binocular rivalry episodes got significantly longer: mean±SD of MDPs for 3.75 Hz, 7.5 Hz, 15 Hz and 30 Hz DSA rate were 5.9±5.5, 2.6±2.7, 6.0±9.8, and 2.4±2.3, respectively [$F(1,9)=9.0$, $P<0.02$]. In brief, subjects on ayahuasca were able to maintain much longer horizontal or vertical dominance periods than without it despite the fact that the stimuli were alternating at rates up to almost 2 orders of magnitude faster than their endogenous rivalry rate.

Discussion

We have found that perceptual switches of binocular rivalry occur despite high rates of DSA in ayahuasca-induced hallucinosis. This finding is similar to what was reported in schizophrenic patients (Frecska et al. 2003).

While this study targeted some common mechanisms in schizophrenia and ayahuasca-induced hallucinosis, it should be noted that according to current views, psychosis and ayahuasca inebriation are not equivalent conditions. Psychosis is neither voluntary nor wished for; it is a disorderly mental state over which the subject has no control. In contrast, ayahuasca, when taken in a traditional-ritual manner, induce a state of being characterized by enhanced internal order. Furthermore, experienced

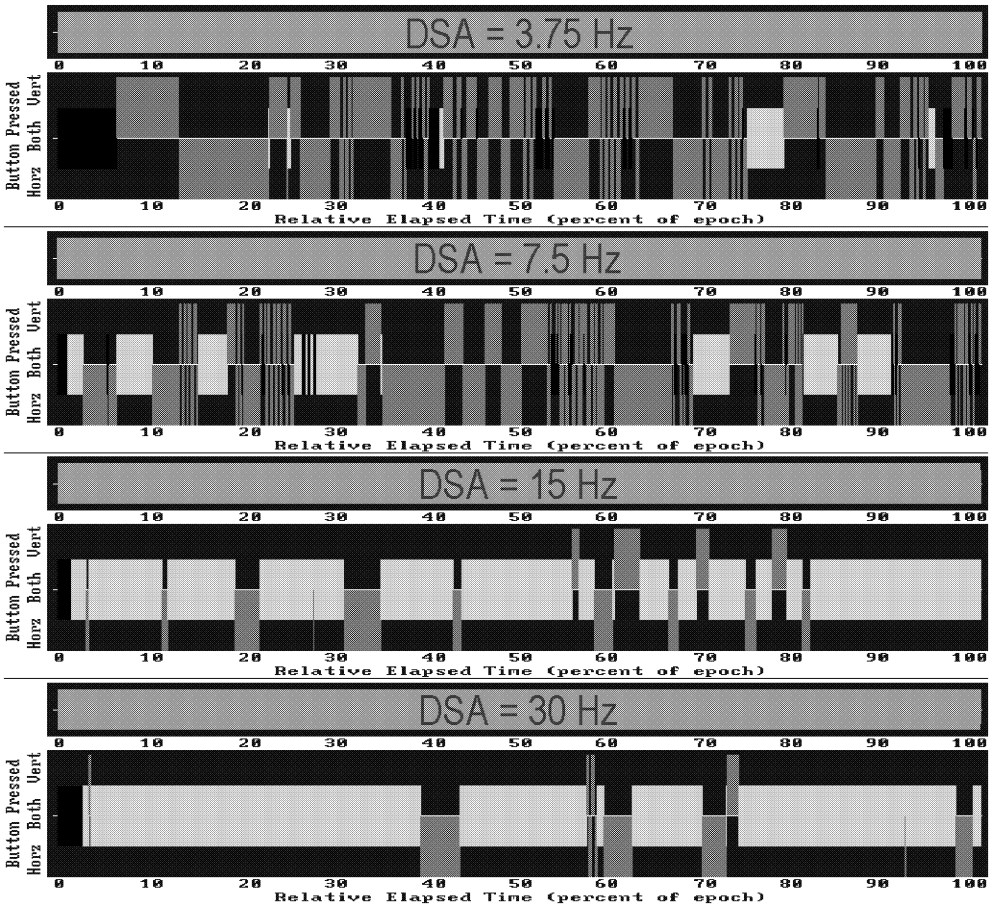

Fig. 3 Typical patterns of perceptual alternation in binocular rivalry at different DSA rates with ayahuasca

ayahuasca drinkers have significant control over what is happening to them under the intoxication (Shanon 2002).

The argument can be made that the response measures we used rely on subjective reports, which might be compromised in some subjects and can be affected by the psychoactive brew. This issue was addressed both by our training procedure and with signal detection analysis, which provided likelihood ratios that the subjects' reports were correct relative to being wrong. All subjects had likelihood ratios significantly greater than the 1:3 ratio for random guessing, as assessed in the pre- and post-experiment "videos". In this way, we emulated binocular rivalry studies in monkeys, who cannot verbally report their perceptual alternations but whose subjective states seem to match those experienced by humans. Moreover, our subjects did not indicate poor performance during video simulations of binocular rivalry while on ayahuasca. No subject's data had to be excluded from analysis due to failure to achieve criterion performance.

A number of visual functions have been reported to be significantly altered by hallucinogenic drugs. These include reduced contrast sensitivity and depth perception (Andre et al. 1994; Leweke et al. 1999), decreased speed of visual processing (Braff et al. 1981), disrupted pre-pulse inhibition (Sipes and Geyer 1997; Jones and Shannon 2000; Javitt and Lindsley 2001; Linn and Javitt 2001; Ouagazzal et al. 2001), poor performance in cognitive tasks involving attention (Jin et al. 1997; Gouzoulis-Mayfrank et al. 2002) and deficit of smooth pursuit eye movements (Ando et al. 1983; Ploner et al. 2002). It has to be noted here that despite a consistently reported decrease of pre-pulse inhibition in animal studies, there is no consensus in the literature on the effect of serotonergic hallucinogens/entactogens on pre-pulse inhibition in humans: with reports on increased (Gouzoulis-Mayfrank et al. 1998; Vollenweider et al. 1999) or lack of effect (Riba et al. 2002). The anomalous visual process that we have described following ayahuasca administration is unlikely to be explained by altered cognitive functions or changes in eye movements. Within each phase of stimulus exposure during DSA at 7.5, 15 or 30 Hz rates, the time is insufficient either for high order information processing or to overcome the latency for initiating smooth pursuit eye movements. Therefore these factors cannot play a determining role in the observed persistence of perceptual alternation. Reduced contrast sensitivity and depth perception have diminishing effects on perceptual rivalry (Cobo-Lewis et al. 2000), and thus provide no explanation.

Considering the limited timeframe, the variation in opinion about the neural mechanism of the relative stability of rivalry in the face of high DSA rates under ayahuasca exposure is then narrowed to early visual processing, so the interpretation of our results will be

presented in that context. We favor the view that an explanation of the persistence of binocular rivalry at high DSA rates requires a neural context that involves the primary visual cortex and visual pathways below. It should be emphasized that this concept is not against the new emerging view that binocular rivalry results from more global processing at higher levels, perhaps coordinated on a hemispheric basis (Pettigrew 2001), with feedback to early visual processing. The model to be presented simply makes an effort to explain how the neural transition of the DSA stimuli escapes steps of regular processing at the "bottom" and becomes subject of perceptual alternation at the "top".

This model, in its simplest form, has already been outlined in the Introduction for schizophrenic patients. To recap and reformulate: slow perceptual processing, which has been implicated in the background of backward masking deficits (Braff et al. 1981), decreased pre-pulse inhibition (Sipes and Geyer 1997; Jones and Shannon 2000; Javitt and Lindsley 2001; Linn and Javitt 2001; Ouagazzal et al. 2001), disturbed auditory event-related potential (Hampson et al. 1989; Javitt et al. 2000; Riba et al. 2002) observed after administration of hallucinogens, and prevented the intoxicated subject "catching up" to the increased DSA rate. At high DSA rates, successive stimuli may exert masking effect on the preceding ones both in schizophrenic patients (Frecska et al. 2003) and subjects influenced by ayahuasca, resulting in relative insensitivity to the higher DSA frequencies and survival of the rivalry. In this way, binocular rivalry with DSA is conceptualized as a continuous series variant of paired stimulus tests. The presented model can explain the persistence of PDP at high DSA rates; however, it cannot give account for the extended MDP induced by ayahuasca.

There is a similarity of the basic perceptual alterations in hallucinogen-induced conditions to those extensively studied in schizophrenic patients and their first degree relatives (see for review, Light and Braff 1999). This parallel observation permits further elaboration of the model and provides an explanation for the extended MDPs in both schizophrenia and drug-induced hallucinosis. In order to address this problem, we will turn to current research on gamma oscillations. The answer will be provided in frame of the gamma synchrony-related "binding theory" of sensory integration.

Patients with schizophrenia experience a wide range of perceptual changes similar to (and even more consistently reported) what we cited above as effect of hallucinogens. Several authors (Green et al. 1999; Lee et al. 2003) suggest that this variety of perceptual changes can be explained in a parsimonious manner. They refer to a type of convergence that can be observed in the literature regarding the underlying mechanisms of the most commonly used perceptual methods. Firstly, pre-pulse inhibition, auditory event-related potentials and visual backward masking all belong to the class of paired-stimulus tests. Secondly, the middle latency auditory event-related potential (P50) appears to be a subset of the auditory gamma band response (Pantev et al. 1993), it is conceptually related to visual masking (Braff et al. 1991) which is also supposed to have gamma-range oscillations as putative neural correlates (Purushothaman et al. 2000). Thirdly, it has been proposed that deficits on P50 may be associated with suppressed cortical oscillations in the gamma range, and Green et al. (1999, 2003) raised the possibility that the visual backward masking deficits of schizophrenics are also linked to cortical gamma oscillations. Oscillations in the gamma range (30–70 Hz) are found over multiple cortical areas and thought to be involved with feature binding (Alais et al. 1998), attentional processes (Singer 1993), motor response preparation (Farmer 1998), and working memory (De Pascalis and Ray 1998). The concept emerges that subtle problems in the gamma range, such as slow frequency undamped waves, prematurely timed early (first burst) or blunted late (second burst) event-related gamma activity might represent the earliest step in a cascade of events leading to deviations in perceptual processing (Green et al. 2003) and other anomalies of integrative brain function (i.e. altered "binding") (Lee et al. 2003).

It has been demonstrated that gamma-frequency synchronization in the visual cortex (V1 and V2) correlates with stimulus selection during binocular rivalry (Fries et al. 2002). According to these authors, both stimulus selection and suppression during dichoptic stimulus presentation is an active process and depends on intact post-retinal gamma-frequency synchronization. It is the relative increase in gamma synchronization of the selected response over the non-selected one that enhances the probability that the given stimulus impacts target neurons at higher processing levels and thereby gains perceptual dominance. One rivaling, but suppressed stimulus can overcome the currently dominant stimulus by power increase in its induced gamma oscillation at V1 and V2. Therefore, binocular rivalry is dependent on alternating increases in gamma synchronization at the visual cortex. We argue that in case of erratic gamma activity, a stimulus can remain dominant for a longer period, since it may take more time for the rivaling stimulus to get beyond the threshold in increased gamma synchronization. There is report on disruption of synchronous interhippocampal gamma oscillations by the hallucinogen mescaline (Doheny and Whittington 1998). We suppose that similar ayahuasca-induced aberration in post-retinal gamma synchronization results in the observed increase in MDPs.

The investigation of the gamma band deficits in hallucinating and/or psychotic individuals is in an early phase yet. Several issues need further clarification. For example, the question can be raised: what kind of visual channels are involved in the discussed phenomenon? Preliminary findings imply that gamma abnormalities are at least partly responsible for visual masking deficits in schizophrenia (Green at al. 2003). The described differences in gamma activity are supposed to originate from the sustained channels (Purushothaman et al. 2000). However, those are subtle compared with the overall

group differences in masking performance. The major component of the early visual deficit in schizophrenia and in drug-induced hallucinosis may derive from other mechanisms, and perhaps due to abnormal processing in the transient channels with uncertain gamma origin. Another series of questions can address the type of gamma pattern change. Most of the studies have focused primarily on reduced gamma power but increased gamma activity was proposed to mediate excessive information processing, i.e. increased "binding" (for review, see Lee et al. 2003), and unsteady frequency is evident behind the sustained visual channel problem in schizophrenia (Green et al. 1999).

In summary, it is premature to specify exactly what kind of underlying neural mechanism can explain the perceptual alterations observed by the use of paired-test procedures and binocular rivalry with DSA. Moreover, according to our knowledge, limited information is available about hallucinogen action on gamma band activity. Our findings are preliminary, our explanation is tentative, but we hope that this study will promote further studies into the field and that the method of binocular rivalry with different stimulus presentations may turn out to be a valuable tool for studying gamma activity-related perceptual functions and dysfunctions. Studies on abnormal gamma activity and its mechanisms may provide an interpretive framework for understanding hallucinogen related breakdown in integrative function.

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