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Pharmacology, Biochemistry and Behavior 75 (2003) 789–793
PHARMACOLOGY BIOCHEMISTRY AND BEHAVIOR
www.elsevier.com/locate/pharmbiochembeh

Reduced binocular depth inversion in regular cannabis users

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Received 9 April 2003; received in revised form 12 May 2003; accepted 20 May 2003

Abstract

The binocular depth inversion illusion (BDII) has been shown to be a sensitive measure of impaired visual information processing under conditions including cannabinoid-intoxicated states, alcohol withdrawal, sleep deprivation, and in patients with positive symptoms of schizophrenia. This study assessed whether the BDII could detect subtle cognitive impairment due to regular cannabis use by comparing 10 regular cannabis users and 10 healthy controls from the same community sources, matched for age, sex, and premorbid IQ. Subjects were also compared on measures of executive functioning, memory, and personality. Regular cannabis users were found to have significantly higher BDII scores for inverted images. This was not due to a problem in the primary processing of visual information, as there was no significant difference between the groups for depth perception of normal images. There was no relationship between BDII scores for inverted images and time since last dose, suggesting that the measured impairment of BDII more closely reflected chronic than acute effects of regular cannabis use. There were no significant differences between the groups for other neuropsychological measures of memory or executive function. A positive relationship was found between EPQ-R-psychoticism and cannabis, tobacco, and alcohol use. Cannabis users also used significantly larger amounts of alcohol. However, no relationship was found between BDII scores and drug use other than cannabis or psychoticism. Compared to the other neuropsychological tests used, the BDII appears to be a more sensitive tool for the detection of subtle impairments in visual information processing related to chronic cannabis use.

Keywords: Cannabis; Visual perception; Binocular depth inversion; Cognitive impairment

1. Introduction

"Binocular depth inversion" describes an optical illusion that normally occurs when a three-dimensional (3D) object is represented pseudoscopically (i.e., visual information intended for the left eye is presented to the right eye and vice versa). Representing an object in this way has the effect of inverting the object, so that a face, for example, should appear concave. Under normal conditions however, the face will nevertheless be perceived as being convex. It is hypothesised that "adaptive" or "top down" processing in perceptual networks is able to adjust the possible contents of perception to be consistent with actual current contexts and past experiences. In this way, implausible sensory data (e.g., "the face is hollow") are internally corrected.

Impairment of such adaptive systems for internal correction has been suggested to explain the disintegrative and reality-impairing properties of psychotic disorders (Schneider et al., 1996b; Malenka et al., 1982; Frith and Done, 1988, 1989). In the case of the binocular depth inversion illusion (BDII), it would be predicted that an individual with impairment of "top down" processing would be less likely to perceive depth inverted images as "normal" and more likely to see them as "hollow". Indeed, it has been shown that in patients with schizophrenia (Emrich, 1988; Schneider et al., 1996b, 2002), the illusion is less likely to occur, particularly when there are active positive symptoms. Similar results have also been found in other "pro-psychotic" conditions such as cannabinoid-intoxicated states (Emrich et al., 1991, 1997; Leweke et al., 1999), alcohol withdrawal (Schneider et al., 1996a, 1998) and sleep deprivation (Schneider et al., 1996b; Sternemann et al., 1997), where it is not unusual for individuals to report psychotic symptoms such as delusional ideas or misperceptions.

In this study we looked at how regular cannabis use affects perception of BDII. Previous studies have shown the acute effects of taking cannabis resin (Emrich et al., 1991),

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doi:10.1016/S0091-3057(03)00140-0

dronabinol (Leweke et al., 1999), nabilone and cannabidiol (Leweke et al., 2000) on perception of BDII. However, no study has looked at the effects of chronic regular cannabis use. Early reviews of the neuropsychological effects of chronic cannabis use concluded that cannabis probably did not produce significant impairment, but that subtle impairment could not be ruled out (Wert and Raulin, 1986). More recent reviews support the occurrence of a "drug residue" effect on attention, psychomotor tasks, and short-term memory during the 12–24 h period immediately after cannabis use (Pope et al., 1995). There is also accumulating evidence for persistent, chronic, complex but subtle cognitive impairments related to frequency and duration of cannabis use (Solowij et al., 1995). These include the organisation and integration of complex information involving various mechanisms of attention and memory (Solowij, 1998). We hypothesised that the BDII, with highly familiar stimuli (faces), would be sufficiently sensitive to demonstrate any subtle cognitive impairment, compared to other neuropsychological tests, in regular cannabis users.

2. Methods

2.1. Subjects

Ten regular cannabis users and 10 healthy controls, with no history of cannabis use, participated in the study. All subjects gave written informed consent to participate in the investigation and the study protocol was approved by the appropriate local ethics committee. All participants were drawn from the same community sources and were matched for age, sex, and premorbid IQ (see Table 1.) Regular cannabis use was defined as using the drug every day, or every other day, for at least a year. Volunteers with a history of regular use (more that 1–2 times per month) of drugs other than cannabis were excluded from the study. All subjects were interviewed using a semistructured questionnaire to enquire about patterns of drug use and past medical and psychiatric illness. Subjects were excluded if they had any history of psychiatric or serious medical illness, including significant head injury and other neurological disorders. As a group, the cannabis users recruited had started smoking cannabis at a mean age of 17.5 ± 1.7 years, had been using for 6.0 ± 2.0 years, and currently consumed 14.2 ± 8.6 joints per week. Other drugs that were used occasionally included MDMA [ecstasy] ($n = 6$), cocaine ($n = 4$), amphetamine ($n = 1$), and psilocybin [mushrooms] ($n = 1$).

Table 1
Demographic data and characteristics of control and cannabis using subjects

Characteristic	Control subjects ($n = 11$)	Cannabis users ($n = 10$)
Male: female ratio	8:3	8:2
Age (years)	23.1 (0.9)	23.5 (2.5)
Years in education	18.2 (0.9)	18.3 (1.2)
Full scale IQ	115.1 (7.7)	120.1 (2.8)
Alcohol (units/wk)	13.5 (6.4)	27.8 (16.0)*
Cannabis (joints/wk)	–	14.2 (8.6)
Time since last dose (h)	–	5.6 (6.6)

All measures reported as: mean (standard deviation).
* $P = < .05$.

2.2. Neuropsychological testing

Neuropsychological testing included the national adult reading test (NART) to measure premorbid IQ; Stroop Colour Interference Test, trail making test, word generation tasks and WIMS (digit span) to test executive functioning and memory; and Eysenck's Personality Test (revised) [EPQ-R] to measure personality dimensional traits.

2.3. Testing stereopsis

Stereoscopic vision was tested using a random-dot stereogram presented on a computer screen. Shutter glasses, synchronized to the screen refresh rate, allowed separate left and right images to be viewed by the respective eyes, due to rapid alternation of the images on the screen.

2.4. Binocular depth inversion

For testing binocular depth inversion, stereoscopic pairs of images were created using a digital camera (see Fig. 1.) There was a disparity of nine degrees between each pair (comparable to binocular disparity). An NVIDIA graphics card and software were employed to combine the stereo pairs to create a 3D image when viewed through the shutter glasses. The stereo images were either normal or depth inverted. Depth inversion was achieved by swapping the images such that the original left-eye image was delivered to the right eye and vice versa. Only images of faces were used as previous studies have shown that the illusion is more pronounced for objects with a high degree of familiarity, particularly faces. Five different faces (four males, one female) were presented in a random order to the subjects in both normal and pseudoscopic form. Depth perception was measured with a scoring system adapted from previous published studies using the BDII (Leweke et al., 1999). The subjects were asked to describe the image in terms of depth of the nose, forehead and overall impression, using the terms "clearly convex", "convex", "flat", "concave" and "clearly concave". A mark between zero and four was awarded for each description, on a five-point rating scale. For each feature a maximum score of four could be achieved, for clearly identifying the true depth, with zero points awarded for complete perceived inversion. Total inversion scores were expressed for each subject as the sum of the scores for each feature, divided by the maximum possible score, giving a range of 0 (*total depth*

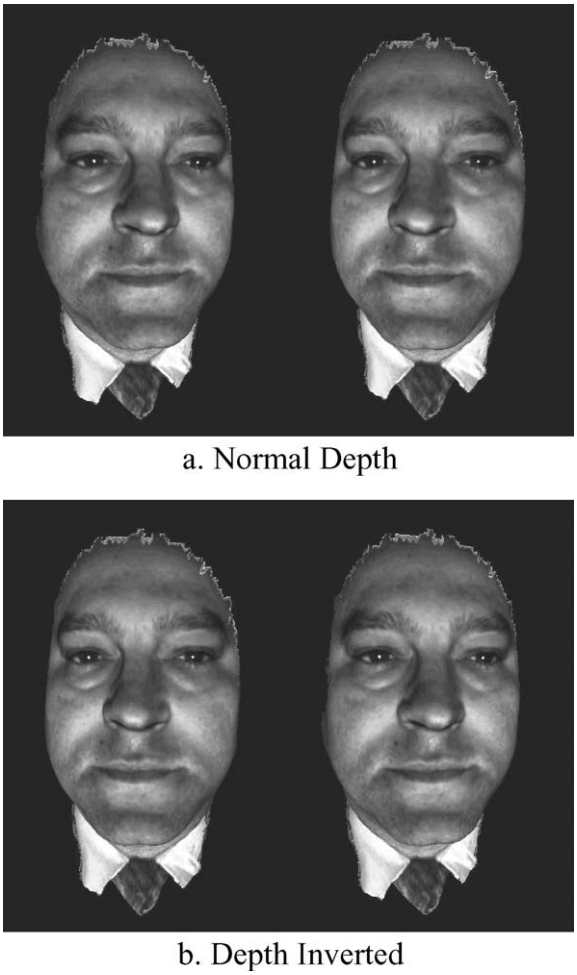

Fig. 1. Examples of stereo images used (normal perspective view). a) Normal depth; b) depth inverted.

inversion) to 1 (*correct depth perception*). Each feature (nose, forehead, overall impression) carried equal weight in the total score.

2.5. Statistical analysis

Statistical analysis of the data was performed using SPSS (Statistical Package for Social Sciences). Mean BDII scores were compared between groups using a Student's *t* test. Where a significant effect was found, backward entry linear regression analysis was performed to examine whether the effect on BDII scores was robust after several covariates (tobacco, alcohol, psychoticism) had been taken into account. Regression analysis allowed the contribution of multiple variables to be modeled for both the BDII scores and other neuropsychological test results.

3. Results

Regular cannabis users were found to have significantly higher BDII scores for inverted images (P=.04), suggesting that the illusion of "normal" depth was less pronounced (see Table 2). This does not appear to be due to a problem in the primary processing of visual information, as there was no significant difference between the groups for depth perception of normal images (P=.14). There was no relationship between BDII scores for inverted images and time since last dose (P=.654). This suggests that the measured impairment of BDII more closely reflected chronic than acute effects of regular cannabis use. A positive relationship was also found between EPQ-R-psychoticism and cannabis (P=.036), tobacco (P=.01), and alcohol use (P=.001). EPQ-R-psychoticism was not, however, related to BDII scores (P=.416). There was a trend towards significance for the relationship between cannabis use and WIMS digit span (P=.05). Further analysis of covariance revealed that this might be explained by the higher rates of tobacco use in the cannabis-using group. No significant relationship was found between BDII scores and other current drug use (e.g., alcohol [P=.896], tobacco [P=.085], MDMA [P=.129], cocaine [P=.889]). Backward entry linear regression analysis demonstrated that the group effect on BDII scores was robust, taking into account the possible covariates of tobacco use, alcohol use, and EPQ-R-psychoticism.

Table 2
Summary of neuropsychological tests

Test	Control subjects (n=11)	Cannabis users (n=10)	t-Test significance
FAS Word Generation Task			
Total score	46.7 (9.2)	51.5 (13.4)	0.36
TRAILS A			
Total time (s)	22.5 (5.5)	26.8 (8.3)	0.19
Errors	0.09 (0.3)	0 (0)	0.34
TRAILS B			
Total time (s)	48.6 (12.8)	47.2 (9.5)	0.77
Errors	0.3 (0.5)	0.2 (0.6)	0.77
WIMS (Digit span)			
Total score	17.3 (2.1)	19.9 (2.6)	0.05
STROOP			
Total time (s)	39.5 (10.4)	45.4 (10.4)	0.21
Errors	0.3 (0.5)	0.5 (1.0)	0.51
EPQR			
Psychoticism	2.4 (2.1)	4.5 (2.2)	**0.04** *
Extraversion	7.5 (2.9)	8.5 (3.6)	0.48
Neuroticism	4.8 (2.2)	3.9 (3.8)	0.52
Lie scale	3.2 (1.7)	2.3 (1.5)	0.22
BDII Test–total scores for "true" depth			
Normal images	0.86 (0.15)	0.77 (0.12)	0.14
Depth inverted images	0.38 (0.13)	0.53 (0.13)	**0.04** *

All measures reported as: mean (standard deviation).
* P= < .05.

4. Discussion

In this study BDII scores for depth-inverted images appear to be a more sensitive measure of "subtle" cognitive deficits related to chronic use of cannabis than the other neuropsychological measures employed. Although measures of EPQ-R-psychoticism were higher for the cannabis-using group, they correlated with other "risk-taking" behaviours (i.e., tobacco and alcohol use), and were independent of BDII scores, suggesting that the differences in BDII scores were related to the effects of regular cannabis use, rather than reflecting premorbid personality traits. The cannabis-using group also used other substances, particularly alcohol, to a greater extent than the control group. Despite this, no significant relationship was found between the use of substances other than cannabis and BDII scores. Selection criteria specifically excluded volunteers whose regular use of illicit drugs other than cannabis was more than 1–2 times per month. These facts make it unlikely that the significant difference in BDII scores between the groups could be explained by the current use of other substances.

As far as possible, confounding factors were taken into account, however, no objective measures of drug use were employed, and we relied upon self-reported histories of drug use. Equally, although the subjects were closely matched (for age, sex, IQ, etc.) the number in each group was small, and there was no period of observed abstinence prior to testing. Despite these drawbacks, there was a significant difference in BDII scores for depth-inverted images between the cannabis-using group and the controls, with no evidence of a relationship between BDII score and time since last use of cannabis.

The cognitive impairment due to chronic regular cannabis use appears to effect adaptive systems involved in the internal correction of ambiguous sensory information. Dysfunction within such systems may explain the increased likelihood of an individual, who regularly uses cannabis, experiencing psychotic phenomena such as misperceptions or delusions. Although the functional anatomical correlates for correction of ambiguous sensory information have yet to be elucidated, there is evidence that both the acute and chronic use of cannabis leads to alterations in frontal lobe functioning, and associated networks (Lundqvist et al., 2001). The similarity between functional networks impaired by cannabis use and those implicated in the pathogenesis of schizophrenia (Loeber and Yurgelun-Todd, 1999) has been suggested to potentially explain the biological basis for cannabis being a possible independent risk factor for the occurrence of schizophrenia-like psychosis or psychotic symptoms (Zammit et al., 2002; Andreasson et al., 1987). This hypothesis is underlined by a recent study showing that the BDII is less likely to occur in patients with active positive symptoms of schizophrenia, with the illusion of normal depth returning when these symptoms are successfully treated with antipsychotic medication (Schneider et al., 2002). Indeed, persons with a high genetic risk of schizophrenia may be more vulnerable to the "psychotogenic" effects of cannabis (Miller et al., 2001).

As yet, there have been no studies utilising the BDII in schizophrenic individuals who use or do not use cannabis, although this clearly would be an interesting avenue for further research: the BDII may represent a useful tool for the early detection of subtle impairments in neural circuits involved in information processing which might help predict onset or relapse of psychotic symptoms, and allow early intervention. At the very least, the BDII appears to be a sensitive measure of cannabinoid-induced cognitive impairment.

Acknowledgements

The authors would like to acknowledge Gordon Watson, Research Consultant, Edinburgh Virtual Environment Centre, for assistance with production of stereo images, the Stanley Medical Research Institute for equipment costs, and Prof. Eve C. Johnstone for support and encouragement.

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