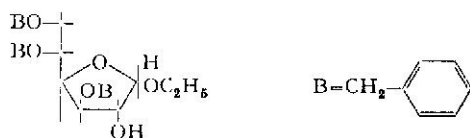


fizierten Mäusen³ in einem Dosenbereich von 10–25 mg/kg s.c. (b) Antiallergische Wirkung sowohl gegenüber systemischer Anaphylaxie (Schock) als auch bei cutanen Reaktionen (Arthus; passive cutane Anaphylaxie) in Dosen ab 10–30 mg/kg i.p. bzw. 10–100 mg/kg p.o. (c) Entzündungshemmende Eigenschaften (Dextranödem der Rattenpfote; Lidentzündung des Kaninchens nach intrapalpebraler Endotoxininjektion) in Dosen von 100 bis 300 mg/kg i.p. oder i.v.

Das Präparat kann hergestellt werden, indem die D-Glucose über 1,2:5,6-Di-O-isopropyliden- α -D-glucopyranose in 1,2-O-isopropyliden- α -D-glucopyranose überführt wird. Die aus dieser Verbindung mit Benzylchlorid in alkalischem Medium entstehende 3,5,6-Tri-O-benzyl-1,2-O-isopropyliden- α -D-glucopyranose wird mit äthanolischer Salzsäure behandelt. Das so erhaltene Äthyl-3,5,6-tri-O-benzyl-D-glucopyranosid stellt ein dickflüssiges Öl dar, das im Hochvakuum (Kurzweg-Destillationsapparat) bei 231–240°C (0,008 mm Hg) destilliert.



CIBA 21401 ist ein Anomerengemisch, welches bei Einhaltung strikter Destillationsbedingungen die spezifische Drehung $[\alpha]_D^{20} = -32^\circ$ ($c = 1$, Chloroform) besitzt

und zu 70% aus β -Form und zu 30% aus α -Form besteht. Die zwei Anomeren lassen sich auf chromatographischem Wege trennen und haben folgende optische Drehungen: α -Anomer: $[\alpha]_D^{20} = +21^\circ$; β -Anomer: $[\alpha]_D^{20} = -56^\circ$ ($c = 1$, Chloroform). (Eine biologische Prüfung der beiden Anomeren ergab keine Wirksamkeitsunterschiede.)

Summary. CIBA 21401-Ba, a glucoside derivative (ethyl-3,5,6-O-benzyl-D-glucopyranoside), antagonizes in vitro the smooth-muscle action of a large number of biogenic amines and polypeptides, the accelerated migration of leucocytes induced by endotoxin, and the Schultz-Dale phenomenon. In vivo, the compound shows anti-inflammatory and anti-allergic effects and improves the survival rate of infected mice treated with suboptimal doses of a sulphonamide.

R. JAKES, G. HUBER,
L. NEIPP, A. ROSSI,
B. SCHÄR und R. MEIER

Pharmazeutische Abteilung, Forschungslaboratorien
der CIBA Aktiengesellschaft, Basel (Schweiz),
28. Oktober 1966.

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A Heuristic Model of Creativity

Psilocybin, as well as 2 other psychoanaleptic compounds, mescaline and D-lysergic acid diethylamide (LSD), induces central sympathetic excitation and an experience of exaltation^{1,2}. Increased sensitivity to sensory stimulation is another characteristic effect of these compounds³. No parallel increase in motor activity is induced by these drugs, however, as is the case with psychomotor stimulants such as the amphetamines, though both groups of drugs raise the metabolic rate and the body temperature⁴.

We have reported that after the oral administration of 10–15 mg Psilocybin, there results an approximately 40% reduction in the sensory input necessary for the detection of a just noticeable taste difference^{5,6} and an approximately 50–70% increase in light sensitivity measured in terms of preferential brightness⁷. Simultaneously there is an increase in output functions, as exemplified by the 5- to 8-fold increase in saccadic frequency of the involuntary micronevystagmoid eye movements⁸ and only a 2- to 3-fold gain in freely-chosen finger tapping rate⁹.

We have also observed that volunteers while experiencing Psilocybin-produced exaltation, report entoptic phenomena – or phosphenes or hallucinations – when viewing a white screen in a dark room. We hypothesized then that these entoptic phenomena could be directed by replacing the white screen with a partially deleted printed text. We define directed hallucinations as a recall of past experience (specifically: single symbols, symbol configurations and their patterns in relation to their meaning).

Printed texts were therefore selected, undeleted (as in Figure A), to serve as control, and with 43% and 74%

deleted from the upper part of each line (as shown in Figure B and C). By applying vertical deletion we well exceed in both samples the 50% redundancy, i.e. the asymptotic maximum unilateral relative sequential constraint, of printed English.

We expected that under systemic excitation such partially deleted texts would constitute a sufficient stimulus pattern to be read at least to some extent. 17 college student volunteers were therefore exposed to a 10–12 mg Psilocybin experience in a supportive, non-laboratory home environment, and then 2–4 weeks later tested before the oral ingestion of the drug and about 90 min later, i.e. at the 'peak' of the drug effect. The test consisted of reading the text in Figure A and B prior to drug

¹ A. HOFMANN, J. exp. med. Sci. 5, 31 (1961).

² A. CERLETTI and A. HOFMANN, Lancet 1, 58 (1963).

³ J. S. DA FONSECA, C. CARDOSO, E. SALGUEIRO, and M. L. FIALHO, in *Neuropsychopharmacology* (Vol. 4 of Proc. 4th Coll. Int. Neuropharmacol., Birmingham 1964), p. 315.

⁴ K. OPITZ, H. GRÜTER, and A. LOESER, Archs int. Pharmacodyn. Théor. 167, 183 (1966).

⁵ R. FISCHER, F. GRIFFIN, R. C. ARCHER, S. C. ZINSMEISTER, and P. S. JASTRAM, Nature 207, 1049 (1965).

⁶ R. FISCHER and R. KÄLBING, in *Recent Advances in Biological Psychiatry*, vol. 9 (Ed. J. WORTIS; Grune and Stratton, New York 1966), in press.

⁷ R. M. HILL and R. FISCHER, Psychopharmacologia (submitted Nov. 1966).

⁸ F. W. HEBBARD and R. FISCHER, Psychopharmacologia 9, 146 (1966).

⁹ R. FISCHER, S. M. ENGLAND, R. C. ARCHER, and R. K. DEAN, Arzneimittel-Forsch. 16, 180 (1966).

ingestion and similar texts A, B, and C of another set with the same % deletion at 'peak'. The performances were taped and scored later in the laboratory. Only words which were correctly read were included in the calculation of % correct reading.

Our main results can be summarized in stating that 4 subjects could read significantly more of the deleted texts at the peak of a 10–12 mg Psilocybin-produced experience than under 'no-drug' or control conditions, specifically up to 42% of text C and up to 95% of text B¹⁰.

A surprising result was that only through the use of Psilocybin and the deleted B and C texts were we able to identify a category of subjects who read the largest % of correct words within the shortest time. This category could not be identified by exposing subjects to the reading of undeleted texts.

4 subjects – the more articulate ones – spontaneously reported 'actually' seeing the missing tops of the letters at the peak of the drug experience. Two of them specifically stated that the upper part of the printed words appeared in lighter gray than the rest and were convinced that the photographer had not deleted them properly.

The phenomenon can be described as an increased ability to form closure, as hallucination or as a result of increased anticipation (attention-expectation). Assuming that excitation raises the intensity of stimuli – or in other words reduces the just noticeable sensory difference necessary for perception – the results are not surprising. PRIEBRAM¹¹ believes that graded neural events could account for the 'orienting reaction' of the organism which functions at a high level of awareness during the reading

of deleted texts, especially under excitation. It could be argued that the phenomenon observed is analogous to the optical hologram¹² or the Fourier transformation of an image, where every point in the transformation carries information about the phase and amplitude of every point in the initial image. The seeing of the full text – although 74% of it is not there – can then be regarded as a wave-front reconstruction of the image from a small area of the hologram. It is known that using only part of a hologram results in the formation of a 'ghost image' of the whole 'object'¹³, which in this case would account for the gray appearance of the missing tops of the letters.

It is felt that the reported closure-making under excitation may well be a model of the creative act. Human existence is closure-making, i.e. creation from moment to moment through closure of the organism with his externalized environment¹⁴. It is this closure-making, i.e. the transformation of information to meaning, which is accelerated and enhanced under the psychoanaleptic drug-produced excitation and exaltation. This experience of elaborating an 'affluent' environment is a reflection of one's own organization, i.e. the organization of a self-referential self-organizing system. Self-reference means that the universe is experienced with reference to the self – subjectively – whereas self-organization refers to the ability to rearrange the 'outside' environment – objectively. Artistic creations, symbolic representations which mirror temporalized spaces and spatialized moments, are of no particular survival value; their unique value is that they unite the subjective and objective in both creator and beholder, or in Baudelaire's words, 'L'art a pour tâche de créer une magie suggestive contenant à la fois l'objet et le sujet, ...'¹⁵.

Zusammenfassung. Im Rahmen eines heuristischen Modells und unter dem Einfluss der psychoanaleptischen Droge Psilocybin wird die regulierend-complementierende geistige Tätigkeit untersucht. Gesunde, junge Volontäre vermögen nach oraler Verabreichung von 10–12 mg Psilocybin gedruckte Texte zu lesen, obgleich der obere Teil jeder Zeile bis zu 74% unsichtbar ist.

ROLAND FISCHER and MARSHA ANN ROCKEY

Department of Psychiatry, Division of Behavioral Sciences, College of Medicine, Ohio State University, Columbus (Ohio 43210, USA), October 17, 1966.

¹⁰ As would be expected, the words which were most frequently read were those most frequently occurring in English, such as 'the', 'and', 'it', and those with some particularly unique configuration which, once recognized, could easily be identified again.

¹¹ K. H. PRIEBRAM, in *Macromolecules and Behavior* (Ed. J. GAITO; Appleton-Century Crofts, New York 1966), p. 167.

¹² E. N. LEITH and J. UPATNICKS, *Scient. Am.* 212, 24 (1965).

¹³ P. J. VAN HEERDEN, *Appl. Opt.* 2, 387 (1963).

¹⁴ R. FISCHER, *Ann. N.Y. Acad. Sci.* (Interdisc. Persp. of Time Conf., New York 1966), in press.

¹⁵ Acknowledgments: Presented at the 4th International Colloquium of Psychopathology of Expression, Washington, D.C. April 3–6, 1966. These studies were assisted by U.S. Public Health Service National Institute of Health, General Research Support Grants, administered by the Ohio State University College of Medicine and the Comly Coleman Fund. Our thanks are due to Drs. R. BIRCHER and L. B. ACHOR, as well as to D. BURR, Sandoz Pharmaceuticals, Hanover, N.J., for generously providing us with Psilocybin; to Miss ANN SCHEUNEMAN and Mrs. RUTH WOMERSLEY PEAR for their competent assistance, and to our highly motivated, devoted and unpaid volunteers for their participation in this study.

A So that we can think of an alpha-particle as held to the rest of the nucleus much as a single molecule is held in a drop of liquid; but if it gets a short step away the attractive forces become ineffective and it then flies off, repelled by the electric forces. Now if we were trying to account for the behaviour in terms of classical dynamics, we should say that the emission of an alpha-particle is like the evaporation of a molecule from the liquid. Any molecule

B So that we can think of an alpha-particle as held to the rest of the nucleus much as a single molecule is held in a drop of liquid; but if it gets a short step away the attractive forces become ineffective and it then flies off, repelled by the electric forces. Now if we were trying to account for the behaviour in terms of classical dynamics, we should say that the emission of an alpha-particle is like the evaporation of a molecule from the liquid. Any molecule

C So that we can think of an alpha-particle as held to the rest of the nucleus much as a single molecule is held in a drop of liquid; but if it gets a short step away the attractive forces become ineffective and it then flies off, repelled by the electric forces. Now if we were trying to account for the behaviour in terms of classical dynamics, we should say that the emission of an alpha-particle is like the evaporation of a molecule from the liquid. Any molecule

(A) An 8 line sample of one of the undeleted 184-word control texts (1/6 of original size). (B) The same as above but with 43% of each line vertically deleted. (C) The same text with 74% vertically deleted.