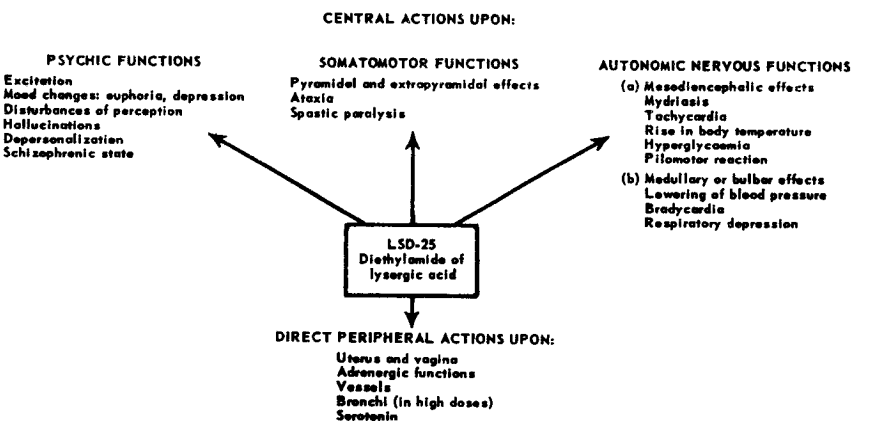
**VI LSD No. 309 (§ 102a)		M 500 effects of LSD
BOL No. 21 (§ 91c)		M 377 psychic effects
LAE No. 11 (§ 102d)		L 256 serotonin antagonism
Hyg	(§ 75m)	M 501 properties of LAE
Meth	(§ 400c)	

ROTHLIN, E. (Pharmacol.Lab., Sandoz, Basle)
Lysergic acid diethylamide and related substances.
Ann.N.Y.Acad.Sc. 66, 668 (1957).

An account of the pharmacological characteristics of LSD and some related compounds. Basically, two different types of action may be distinguished: direct peripheral actions and central actions. These are summarised in the following diagram:



Antagonism to serotonin:

INHIBITION OF SEROTONIN BY VARIOUS AMIDES OF LYSERGIC ACID

1. LSD and its isomers	
d-Lysergic acid diethylamide (=LSD-25)	very active (standard)
l-Lysergic acid diethylamide }	practically inactive, that is, more than 100 times weaker
d+*l*-Isolysergic acid diethylamide }	
2. Derivatives of LSD obtained by saturation of the double bond (C_9 to C_{10})	
Dihydro-*d*-lysergic acid diethylamide	1.6 times weaker
Lumi-*d*-lysergic acid diethylamide	practically inactive
3. Substituted derivatives of LSD	
d-1-Acetyl-LSD	2 times stronger
d-2-Brom-LSD (= BOL 148)	1.5 times stronger
d-2-Iodo-LSD	2 times weaker
d-1-Oxy-methyl-LSD	1.5 times weaker
4. Monosubstituted amides of *d*-lysergic acid*	

Monomethylamide of *d*-lysergic acid	15.5 times weaker
Monoethylamide of *d*-lysergic acid	8.5 times weaker
Monoisopropylamide of *d*-lysergic acid	5.0 times weaker
Monopropylamide of *d*-lysergic acid	2.5 times weaker
Monobutylamide of *d*-lysergic acid	1.5 times weaker
5. Disubstituted amides of *d*-lysergic acid*	
Dimethylamide of *d*-lysergic acid	5 times weaker
Diethylamide of *d*-lysergic acid (= LSD-25)	= standard
Di-isopropylamide of *d*-lysergic acid	4 times weaker
Dibutylamide of *d*-lysergic acid	3 times weaker

* Preliminary results.

The most important of the compounds related to LSD is BOL. The pharmacological actions of the two drugs are compared in the following table:

COMPARISON BETWEEN THE PHARMACOLOGICAL ACTIONS OF LSD AND BROM-LSD

	LSD	Brom-LSD
Rabbit uterus and vagina *in vivo*	Contraction Approximately 1.5 times weaker than ergonovine (ergometrine)	No contraction In higher doses, inhibition of the spontaneous rhythm
Adrenolytic effect (seminal vesicle of guinea pig)	Approximately 50 times weaker than ergotamine	Approximately 5 times weaker than ergotamine
Blood pressure in the cat	Decrease	Very weak action, non-specific
Heart rate	Bradycardia	No effect
Eye, pupil	Mydriasis	No effect
Body temperature:		
Rabbit, dogs, cat	Rise (in all doses)	Decrease in high doses
Rat	Decrease; toxic doses: rise	Decrease (in all doses)
Heat production (calorimeter)	Primarily no increase; secondary rise	Not investigated
Blood sugar	Increased	No change
Behavior of normal mice	Excitation	Sedation
Amphetamine-excitation in the mouse	Potentiated	Inhibited
Effect on waltzing mice	Inhibition of waltzing due to excitation	Inhibition of waltzing due to sedation
Potentiation of pentothal effect in the mouse	Marked	Present but weaker than with LSD
EEG in the rabbit	Activation	No activation
Chromatophores (Poecilia)	Spreading	2.5 times as strong as LSD
Psychic action in man	Very pronounced	Absent
Toxicity L.D.$_{50}$ Mouse *i.v.*	L.D.$_{50}$ 46 mg./kg.	20 mg./kg.
Rat *i.v.*	16.5 mg./kg.	—
Rabbit *i.v.*	0.3 mg./kg.	6 mg./kg.

The drugs exerting psychic effects are depicted in the following diagram as is an assessment of the serotonin antagonism:

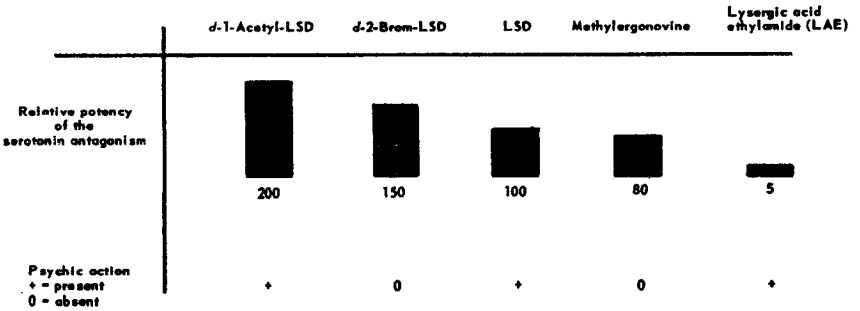


FIGURE 2

The results obtained with BOL make it difficult to correlate the psychic effects of LSD with its serotonin antagonism.

All the compounds that produce psychic changes (LSD, LAE and acetyl-LSD) also exert central autonomic effects. All are due to stimulation of mesencephalic and diencephalic structures and all have a pronounced sympathicotonic character. They are suppressed by ganglion-blocking agents and by Hyg. BOL does not cause this central sympathetic stimulation, which may be considered the counterpart to the central sympathetic depression caused by reserpine (predominance of vagal functions, fall in body temperature, bradycardia, miosis and sedation). Further study will determine whether LSD and reserpine act on the same central mechanism but in different ways and whether their effects can be correlated with one another.

In animals a central sympathicomometic syndrome predominates and psychic changes are probably present but difficult to interpret. In human beings, the psychic changes predominate while the autonomic symptoms are apparently subordinate. It may be assumed that the two actions are not independent of one another.

COMMENT: For a further review of LSD and related compounds see ROTHLIN, LSD No. 382/BOL/LAE/(Gy)/(Hyg).

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(LSD und verwandte Substanzen)

Uebersicht über die Pharmakologie von LSD und ähnlichen Verbindungen. Grundsätzlich hat LSD 2 Arten von Wirkungen: unmittelbar

periphere und zentrale. Bei Tieren überwiegt die Wirkung auf das VNS, aber wahrscheinlich wird auch die Psyche verändert. Beim Menschen sind die Wirkungen auf die Psyche vorherrschend und die vegetativ-nervösen Symptome treten an Bedeutung zurück. Nach den Versuchsergebnissen mit BOL erscheint es schwierig die psychischen Wirkungen von LSD mit dessen Hemmwirkung gegenüber Serotonin in Verbindung zu bringen. Alle Substanzen, welche psychische Veränderungen verursachen (LSD, LAE und Acetyl-LSD) haben auch zentrale vegetativ-nervöse Wirkungen von ausgesprochen sympathicotonem Charakter, welche durch ganglienblockierende Mittel und durch Hyg unterdrückt werden können. Diese zentrale Sympathicusreizung kann als Gegenstück der zentralen Sympathicushemmung durch Reserpin angesehen werden. [Siehe auch ROTHLIN, LSD Nr.382/BOL/LAE/(Gy)/(Hyg).]

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(LSD et substances apparentées)

Revue de la pharmacologie du LSD et de substances apparentées. En principe, le LSD exerce 2 types d'actions: des effets périphériques directs et des effets centraux. Chez les animaux, l'effet sur le SNV est prédominant, mais probablement il y a aussi des modifications psychiques. Chez l'homme, les effets sur le psychisme prédominent, et les symptômes neuro-végétatifs sont moins importants. D'après les expériences faites avec BOL, il semble difficile d'établir une corrélation entre les effets psychiques du LSD et son effet antisérotonine. Toutes les substances provoquant des modifications psychiques (LSD, LAE, et acétyl-LSD) exercent aussi des effets neuro-végétatifs centraux à caractère nettement sympathicotonique qui peuvent être supprimés par des agents ganglioplégiques et par Hyg. Cette stimulation centrale du sympathique peut être considérée comme le pendant de l'inhibition centrale su sympathique provoquée par la réserpine.[V. aussi ROTHLIN, LSD No 382/BOL/LAE/(Gy)/(Hyg).]

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