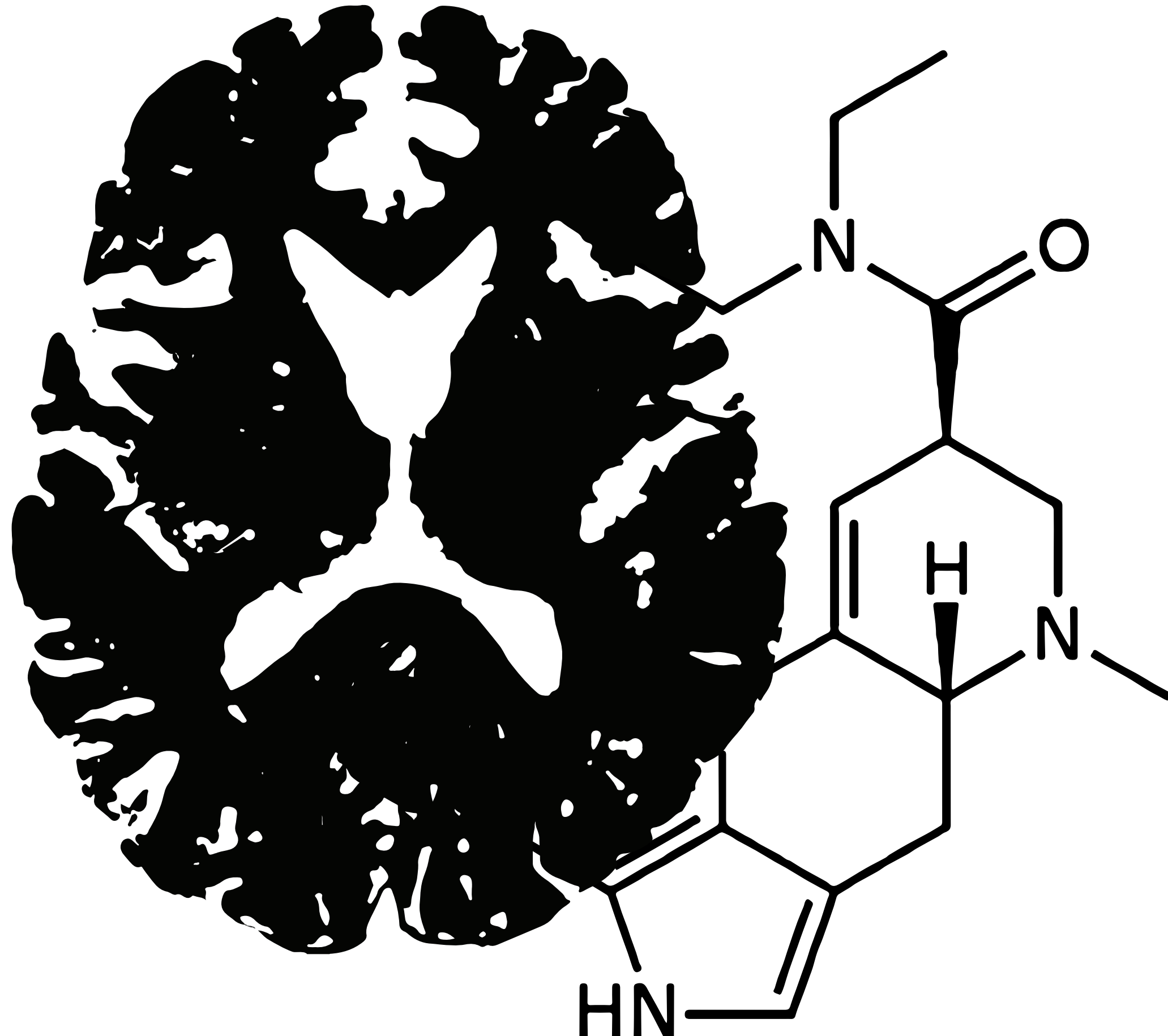


# Drugs: Basics and Hallucinogens



- Describe 4 ways of administering a drug.
- Discuss the history of LSD.
- Describe the LSD trip.
- What is the mechanism of action of LSD?
- Describe the serotonin hypothesis of schizophrenia and the evidence upon which it is based.

# Learning Goals

# What is a drug?

There is no single precise definition. The term “drug” is used by many different people in many different contexts. However, we can at least say the following:

- (1) A drug is assumed to affect physiological functioning in some way.
- (2) It is exogenous (rather than endogenous; e.g., insulin).

# Drug Basics

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Each of the drugs we will be talking about are psychoactive drugs: Drugs that influence subjective experience and behaviour by acting on the CNS.

# Drug Basics

# Drug Administration & Absorption

Drugs are usually administered in 1 of 4 ways:

1. Ingestion. Advantages: Easy and relatively safe. Disadvantages: Unpredictable effects.
2. Injection: Either subcutaneously (SC; into fatty tissue below skin), intramuscularly (IM; into muscle), or intravenously (IV; into vein). Advantages: Speedy and predictable effects. Disadvantages: Speedy effects, infection potential.
3. Inhalation. Drugs are absorbed via the capillaries in the lungs. Advantages: Speedy effects. Disadvantages: Unpredictable effects.
4. Absorption through mucous membranes (nose, mouth, rectum). Disadvantages: Damages membranes.

## Basic Principles of Drug Action

# Drug Penetration of the CNS

Once a drug enters the bloodstream, it is carried in the blood to the blood vessels of the CNS. The blood-brain barrier only allows some blood-borne substances to pass into the CNS.

## Basic Principles of Drug Action

# Mechanisms of Drug Action

Some drugs (e.g., alcohol) act diffusely on neural membranes throughout the CNS.

Others act in more specific ways:

- Binding to particular synaptic receptors.
- Influencing synthesis, transport, release, or deactivation of particular neurotransmitters.
- Influencing the chain of chemical reactions elicited in postsynaptic neurons by the activation of their receptors.

## Basic Principles of Drug Action

# Drug Metabolism & Elimination

The actions of most drugs are terminated by liver enzymes: Drugs are converted from active to inactive forms.

Other sites of inactivation include the gastrointestinal tract, the lungs, and the kidneys.

Drugs are also excreted: urine, sweat, feces, breath, mother's milk.

## Basic Principles of Drug Action



# Drug Tolerance

After you consume a drug repeatedly, you may become tolerant to some of its behavioural effects: Drug tolerance is a state of decreased sensitivity to a drug that develops as a result of exposure to it.

Or you may become sensitized to some of its behavioural effects: Drug sensitization is a state of increased sensitivity to a drug that develops as a result of exposure to it.

## Basic Principles of Drug Action

# Drug Tolerance

Two sorts of changes underlie drug tolerance:

- (1) Metabolic tolerance: Results from changes that reduce the amount of drug getting to its site of action.
- (2) Functional tolerance: Results from changes that reduce the reactivity of the sites of action to the drug.

## Basic Principles of Drug Action

# Drug Tolerance

Tolerance to psychoactive drugs is largely functional and can result from any of several sorts of changes: Exposure to a psychoactive drug can reduce the number of receptors for it, decrease the efficiency with which it binds to those receptors, etc.

## Basic Principles of Drug Action

# Drug Withdrawal

If an animal has been on a drug for a significant period of time, the subsequent removal of the drug will produce a withdrawal syndrome.

## Basic Principles of Drug Action

# Addiction

Drug-addicted persons are habitual drug users who continue to use a drug despite its adverse effects (e.g., health, social life) and despite their repeated efforts to stop using.

Drug addiction should not be equated with physical dependence: Many drug-addicted individuals will resume use of a drug long after they have recovered from the withdrawal syndrome associated with cessation of use of the drug.

## Basic Principles of Drug Action



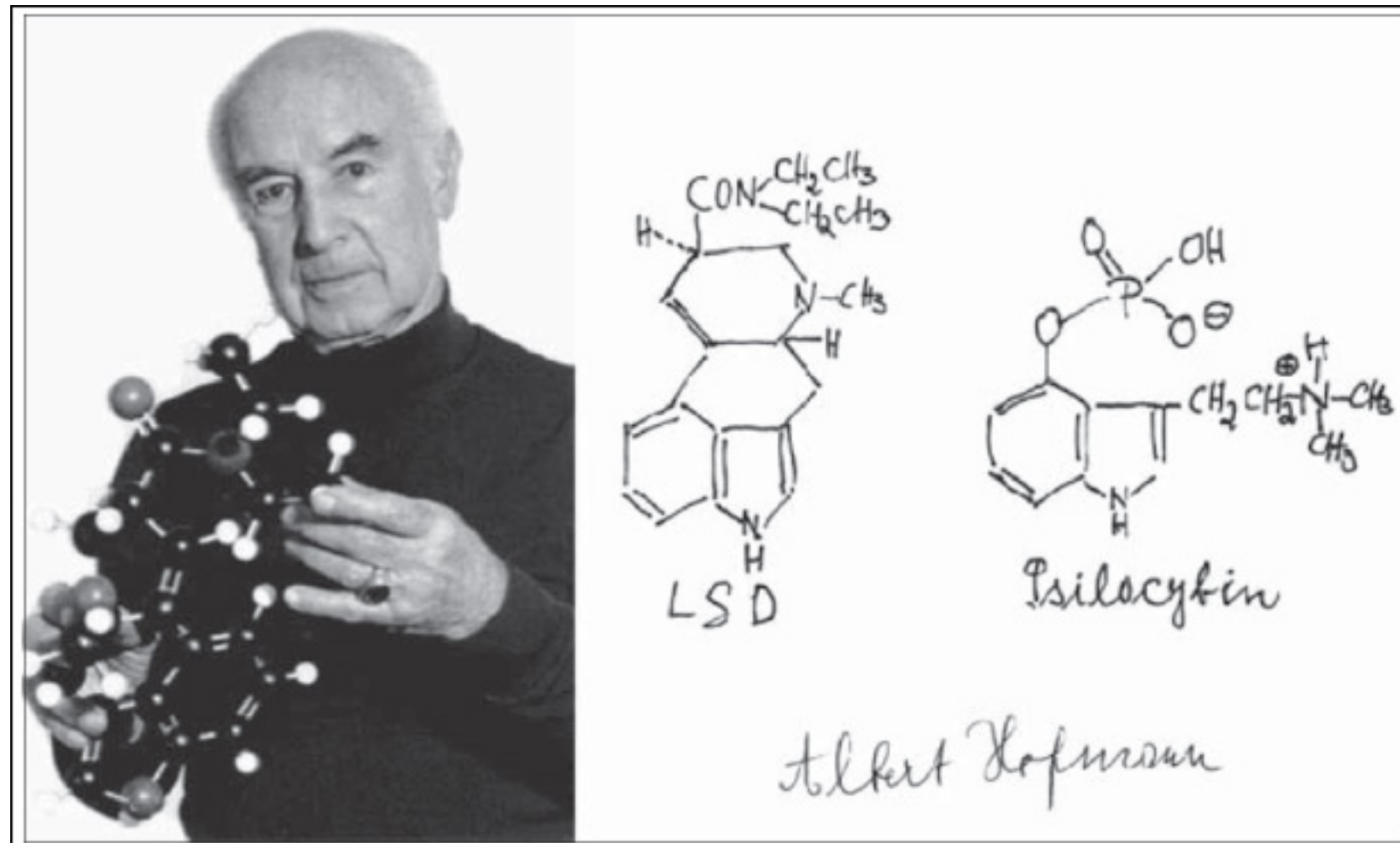
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from Fusar-Poli & Borgwadt, 2008

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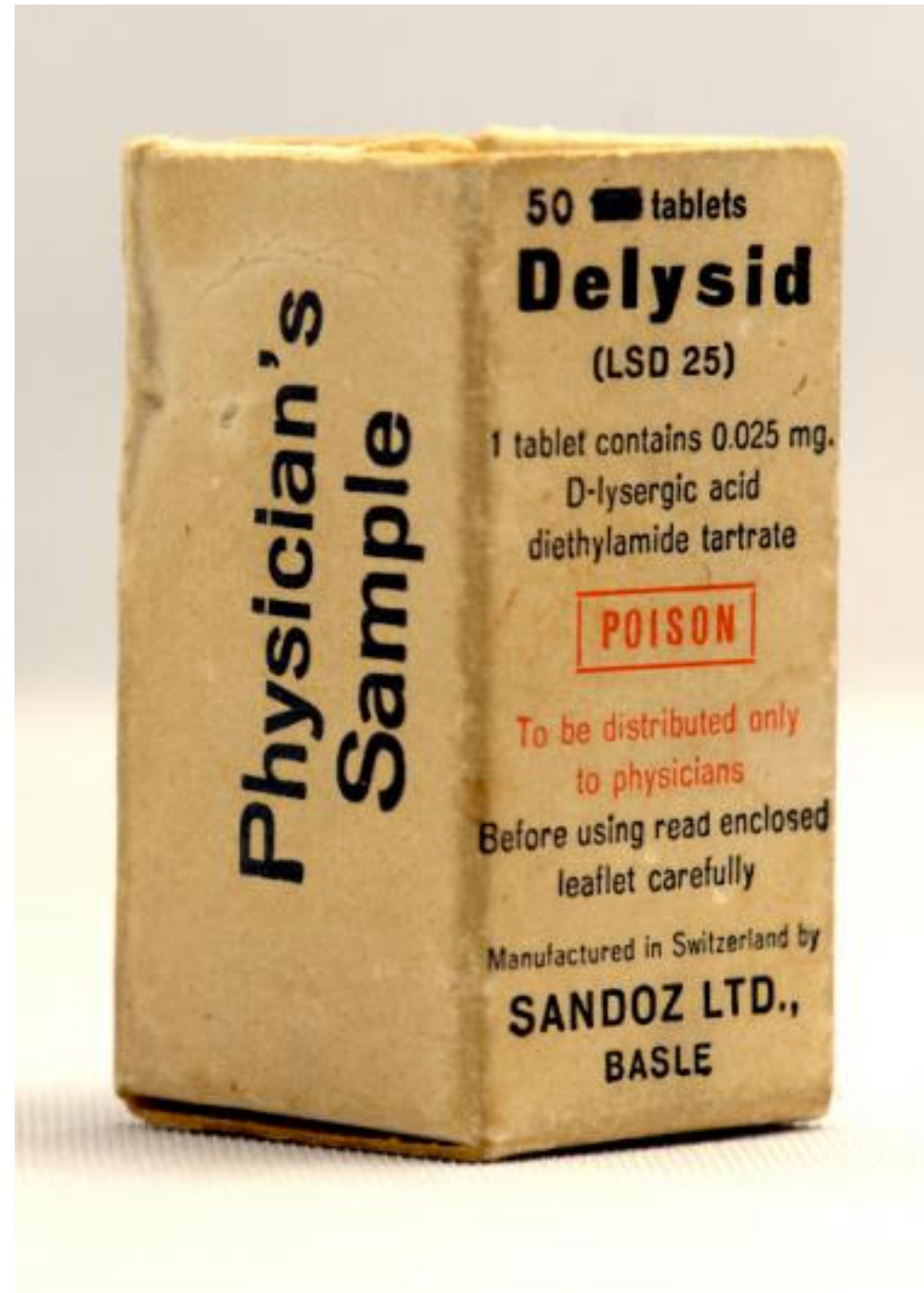
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Hoffman's employer, Sandoz pharmaceuticals, subsequently made the drug freely available for research purposes.

# LSD



# LSD

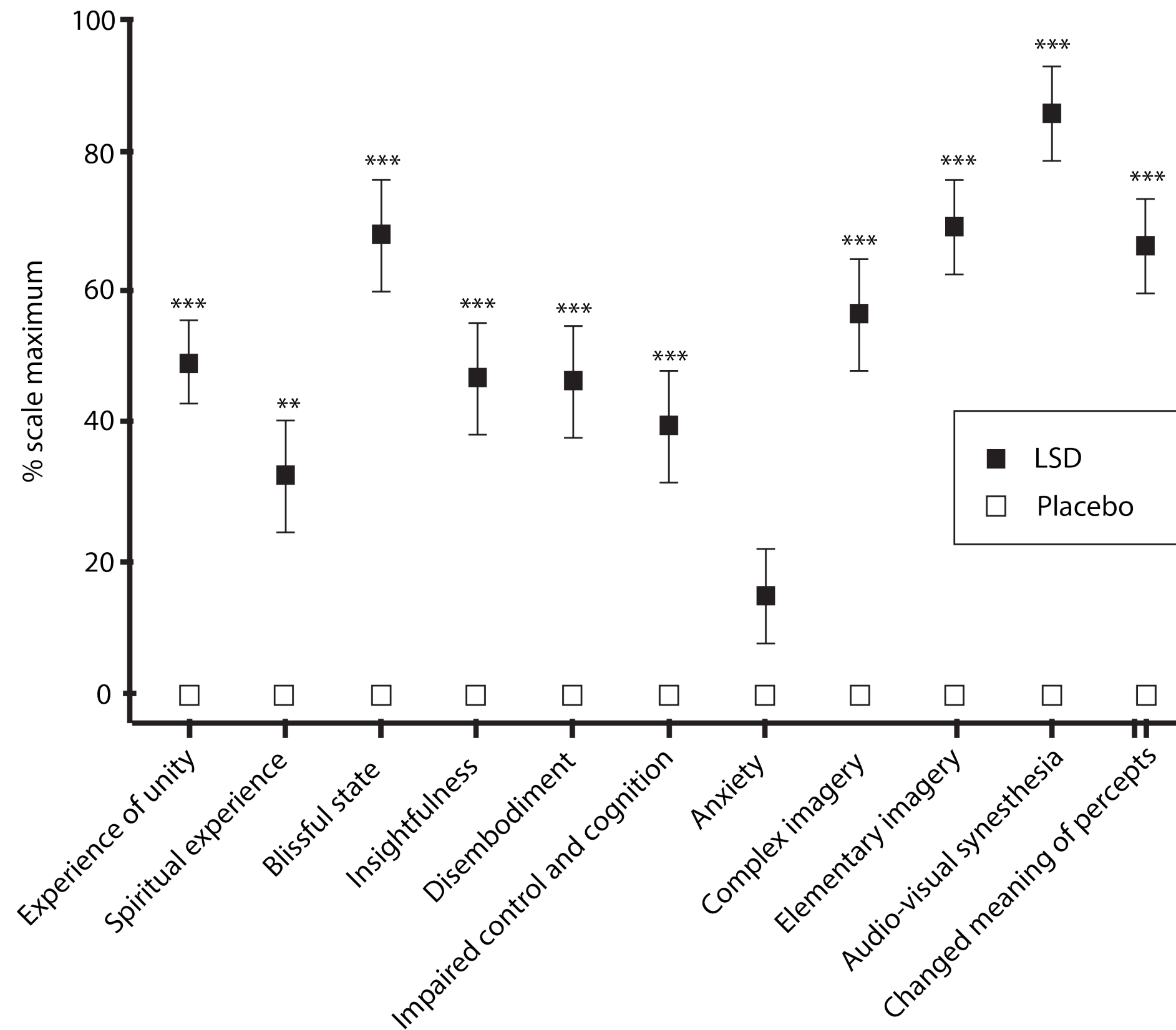




LSD

from Kupferschmidt, 2014

# Subjective Experience



adapted from Schmid et al., 2014

LSD

# Therapeutic Uses

Researchers are investigating the use of LSD to treat a wide variety of ailments.

Some examples:

- anxiety in patients with life-threatening diseases
- cluster headaches
- addiction to alcohol and other substances

LSD

# Mode of Action

LSD shows a strong affinity for serotonergic receptors, with particularly strong excitatory effects at serotonin<sub>2a</sub> receptors.

LSD



# Serotonin Hypothesis of Schizophrenia

Three key points:

1. The psychological effects of LSD are mediated by the serotonin<sub>2a</sub> receptor.
2. Serotonin<sub>2a</sub> receptor abnormalities are evident in the brains of patients with schizophrenia and at-risk individuals.
3. Serotonin<sub>2a</sub> receptor antagonism is known to contribute to the effects of atypical antipsychotics (e.g., clozapine, risperidone).

## Serotonin Hypothesis