

平成20年11月6日

群馬大学行動科学講義 第6回

中枢興奮薬
幻覚薬

● 標準薬理学 第6版

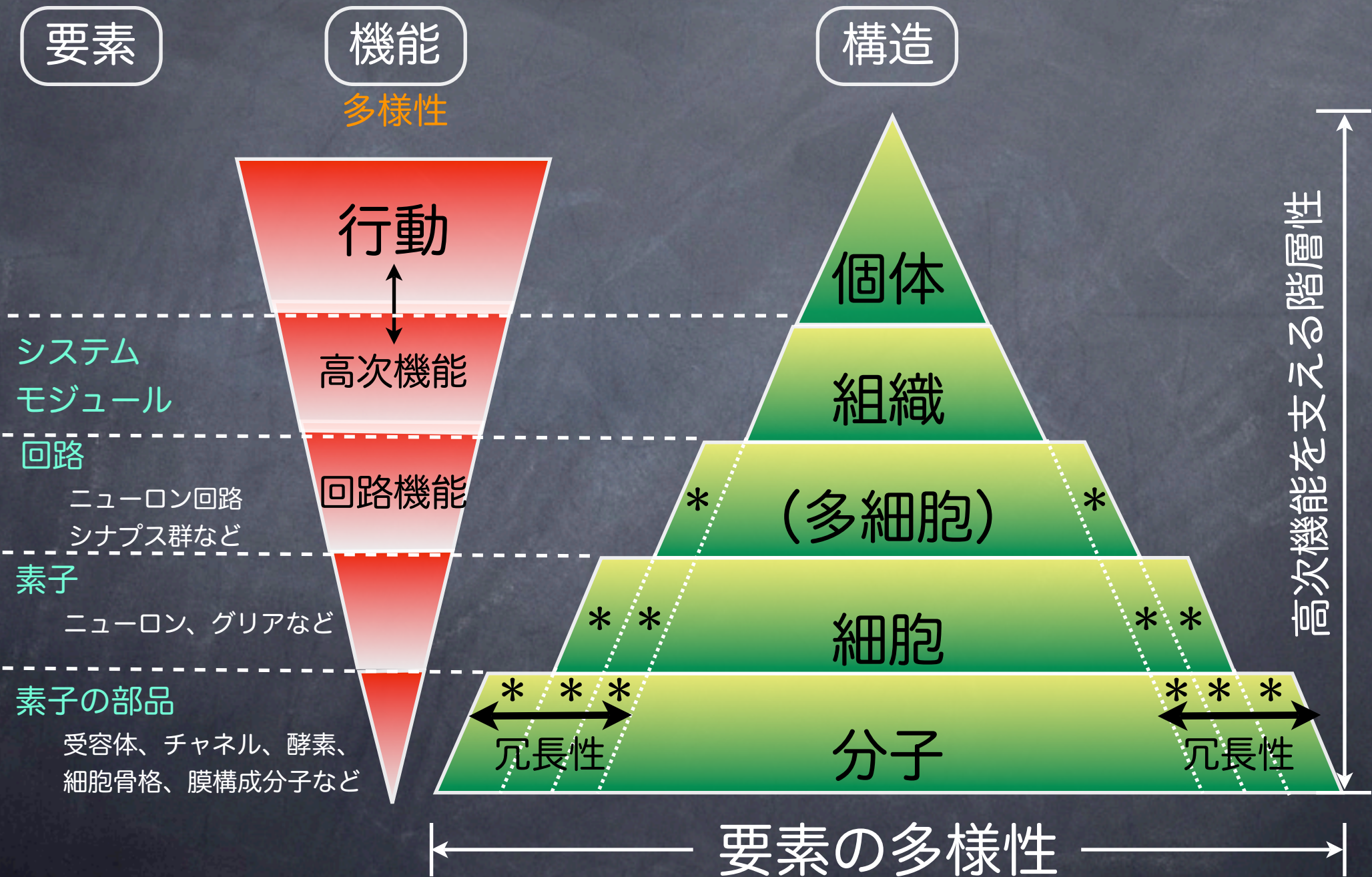
監修 鹿取 信

編集 今井 正 宮本 英七

Science is the art
of the soluble!

In "Plato's Republic" (1982)
by **Peter Medawar**, an immunologist who in 1960
won a Nobel Prize for his innovative study on
transplantation immunity.

脳研究の障壁—脳の多様性と階層性



けいれん薬 convulsants

- picrotoxin
- pentylenetetrazol
- strychnin

蘇生藥 analeptic,

呼吸促進藥 respiratory stimulants

- doxapram

幻覚薬 psychedelics, hallucinogens, psychotomimetics

● リゼルグ酸エチルアミド LSD

5HT_{1A, 1C} アゴニスト

● フェンサイクリジン PCP NMDA antagonist

● メスカリン mescaline

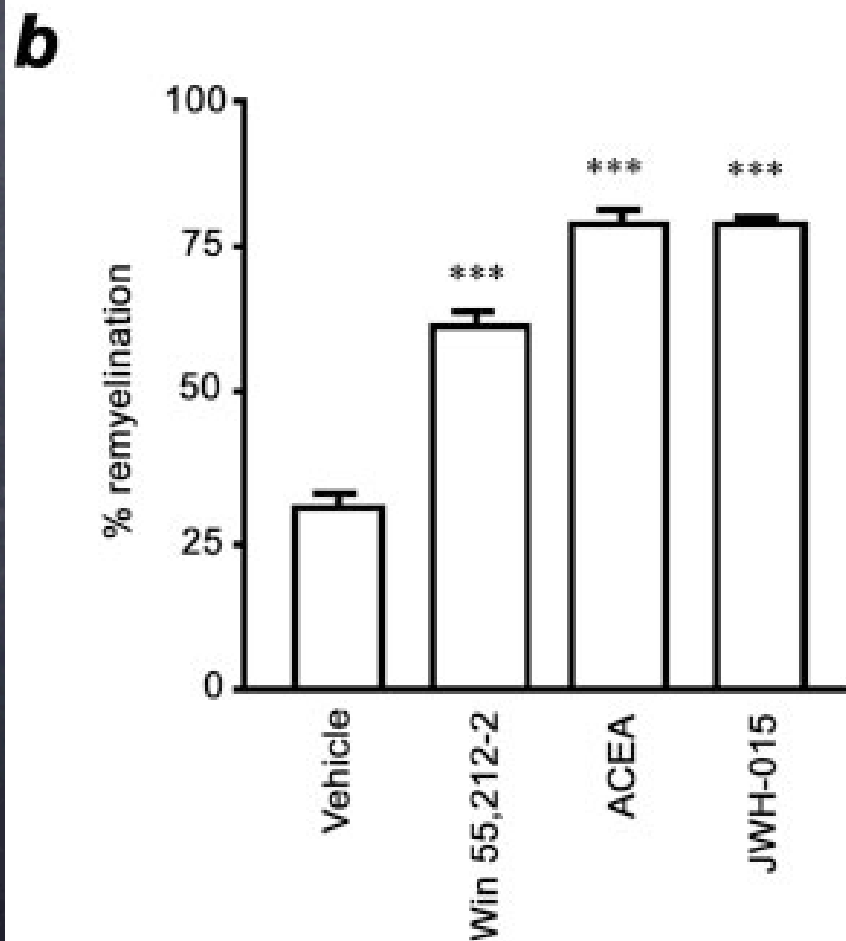
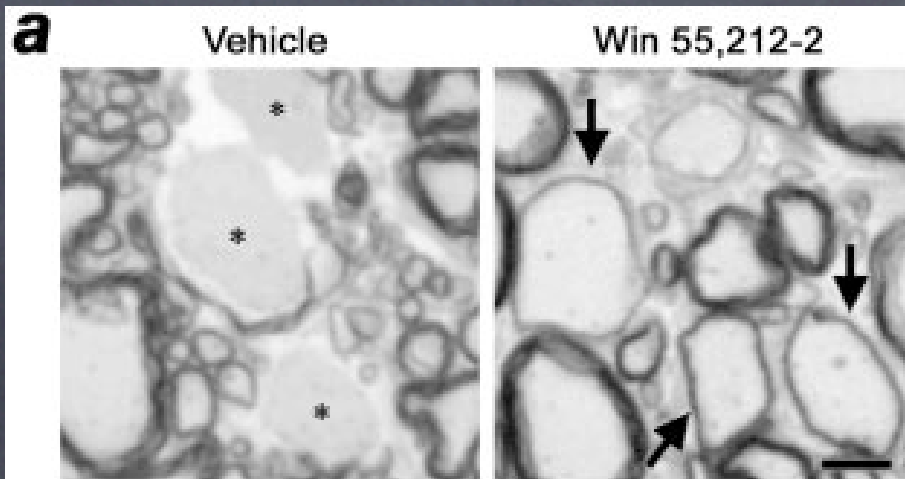
● マリファナ marihuana

● 大麻 cannabinoid

Therapeutic action of **cannabinoids** in a murine model of multiple sclerosis (MS)

Arévalo-Martin et al. JNS 2003, 23(7):2511-2516

- human multiple sclerosis (immune-mediated demyelinating disease) のマウスモデル
- synthetic cannabinoids; WIN55,212-2, ACEA, JWH-015
- cannabinoids reduced microglial activation, MHCII antigen expression, CD4+ infiltrating T cells



Cannabinoids

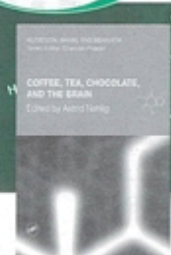


Both recovery of motor function and diminution of inflammation paralleled extensive remyelination.

Methylxanthine系薬

誘導体 caffeine, theophylline, theobromine

- 細胞内 Ca^{2+} の動員 (0.5-1.0 mM)
- cAMP phosphodiesteraseの阻害 (> 50 mM)
- Adenosine受容体の拮抗 (<50 mM)

NEW!**Compelling Insight Into the Connection Between Caffeine and the Brain**

Coffee, Tea, Chocolate and the Brain

Edited by

ASTRID NEHLIG

INSERM, STRASBOURG, FRANCE

A volume in the Nutrition, Brain and Behavior series

Chandan Prasad

LOUISIANA STATE UNIVERSITY, BATON ROUGE, USA

A CLOSER LOOK AT CAFFEINE'S HELPFUL AND HARMFUL EFFECTS

Coffee, tea, and chocolate are among the most frequently consumed products in the world. The pleasure that many experience from these edibles is accompanied by a range of favorable and adverse effects on the brain that have been the focus of a wealth of recent research.

Coffee, Tea, Chocolate and the Brain presents new information on the long-debated issue about the beneficial and/or potentially negative effects on the brain of the consumption of coffee, tea, and chocolate. With caffeine as the common component in these beverages and food, this volume features important data on the effects of caffeine on sleep, memory, cognition, mood, performance, and more. It also contains specific information on new directions of research on the effect of caffeine on Parkinson's disease, seizures, ischemia, the stress axis, and brain development. Debate on the potential addiction to caffeine is included, as well as discussion of how chocolate and caffeine can induce or alleviate various types of headaches.

With contributions from world-renowned experts in the field, this up-to-date reference provides important information for scientists, researchers, industry professionals, and students involved in nutrition, neurology, neuropharmacology, clinical psychology, and other health-related sciences.

FEATURES

- Presents the beneficial and negative effects of caffeine on brain functioning, including therapeutic benefits and caffeine dependency
- Discusses the effects of caffeine on sleep, cognition, memory, performance, and mood
- Includes contributions from internationally renowned specialists

CONTENTS

- Mechanisms of Action of Caffeine on the Nervous System,
John W. Daly and Bertil B. Fredholm
- Effects of Caffeine on Sleep and Wakefulness: An Update,
Jan Snel, Zoé Tieges, and Monique M. Lorient
- Arousal and Behavior: Biopsychological Effects of Caffeine,
Barry D. Smith, Amanda Osborne, Mark Mann, Heather Jones, and Thom White
- Coffee, Caffeine and Cognitive Performance,
Jan Snel, Monique M. Lorient, and Zoé Tieges
- Effects of Coffee and Caffeine on Mood and Mood Disorders,
Miquel Casas, Josep Antoni Ramos-Quiroga, Gemma Prat, and Adil Qureshi
- Age-related Changes in the Effects of Coffee on Memory and Cognitive Performance,
Martin P.J. van Boxtel, and Jeroen A.J. Schmitt
- Neurodevelopmental Consequences of Coffee/Caffeine Exposure,
Tetsuo Nakamoto
- Caffeine Effects on the Human Stress Axis,
Mustafa al'Absi and William R. Lavallo
- Dependence Upon Coffee and Caffeine: An Update,
Astrid Nehlig
- Caffeine and Parkinson's Disease,
Michael A. Schwarzschild and Alberto Ascherio
- Caffeine in Ischemia and Seizures: Paradoxical Effects of Long-term Exposure,
Astrid Nehlig and Bertil B. Fredholm
- Caffeine and Headache: Relationship with the Effects of Caffeine on Cerebral Blood Flow,
Astrid Nehlig
- Effects of Non-caffeine Constituents in Roasted Coffee on the Brain,
Tomas de Paulis and Peter R. Martin
- Can Tea Consumption Protect Against Stroke?,
Astrid Nehlig
- The Biology and Psychology of Chocolate Craving,
David Benton
- Is There a Relationship between Chocolate Consumption and Headache?,
Lidia Savi

See reverse side for Other Titles of Interest and ordering information

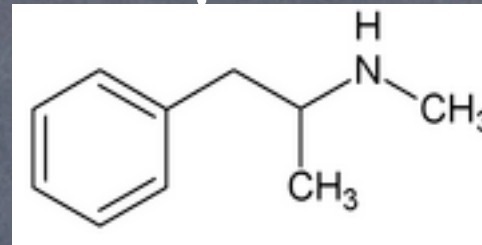
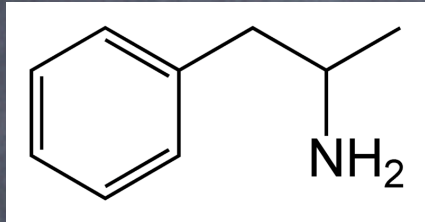
**CRC PRESS**

Catalog no. TF1650, April 2004, 248 pp.
ISBN: 0-4153-0691-4, \$99.95 / £60.99

精神運動刺激薬

psychomotor stimulants

- amphetamine, methamphetamine



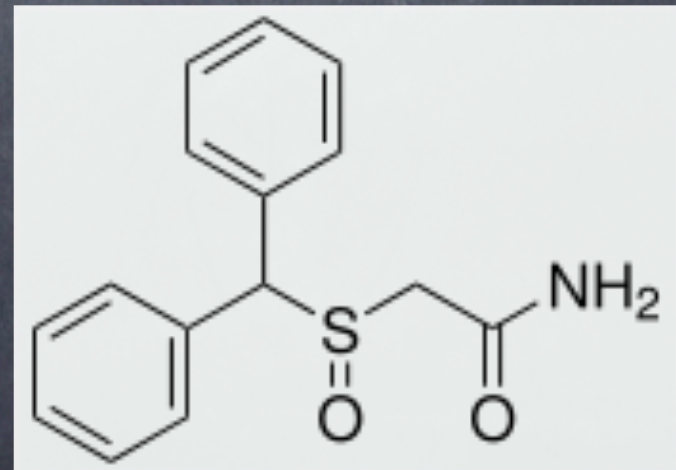
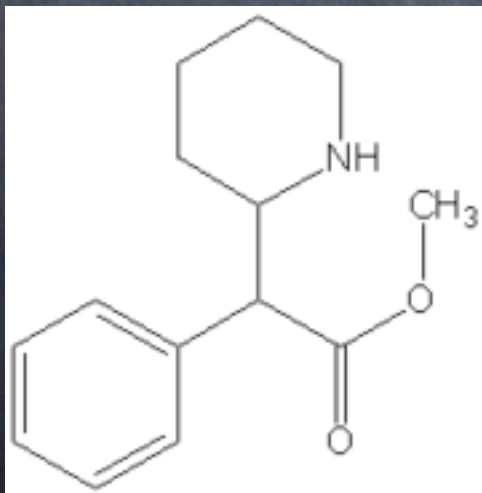
ヒロポン

- methylphenidate

ADHD, Narcolepsy

Methylphenidate

Modafinil (覚醒促進剤)



ナルコレプシー (narcolepsy)

4大症状

- 情動脱力発作 (カタプレキシー)
- 睡眠発作
- 入眠時幻覚
- 睡眠マヒ (金縛り)

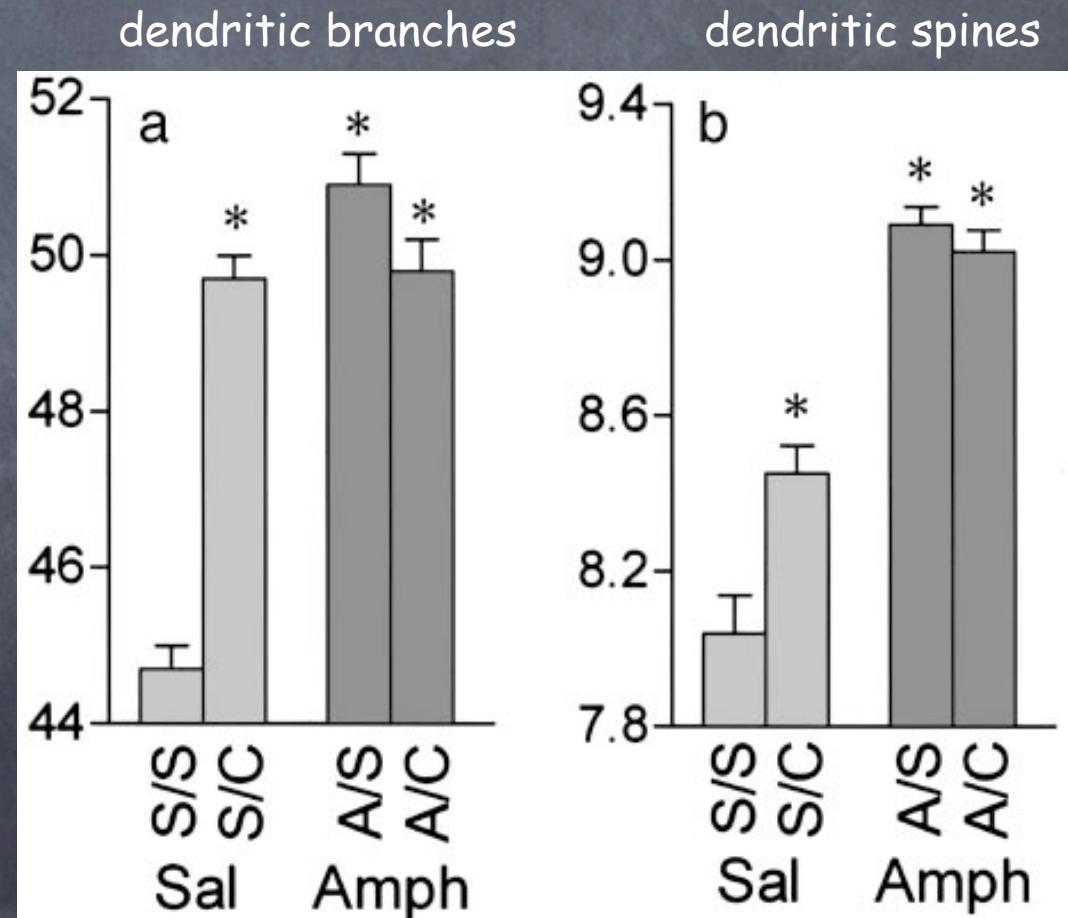
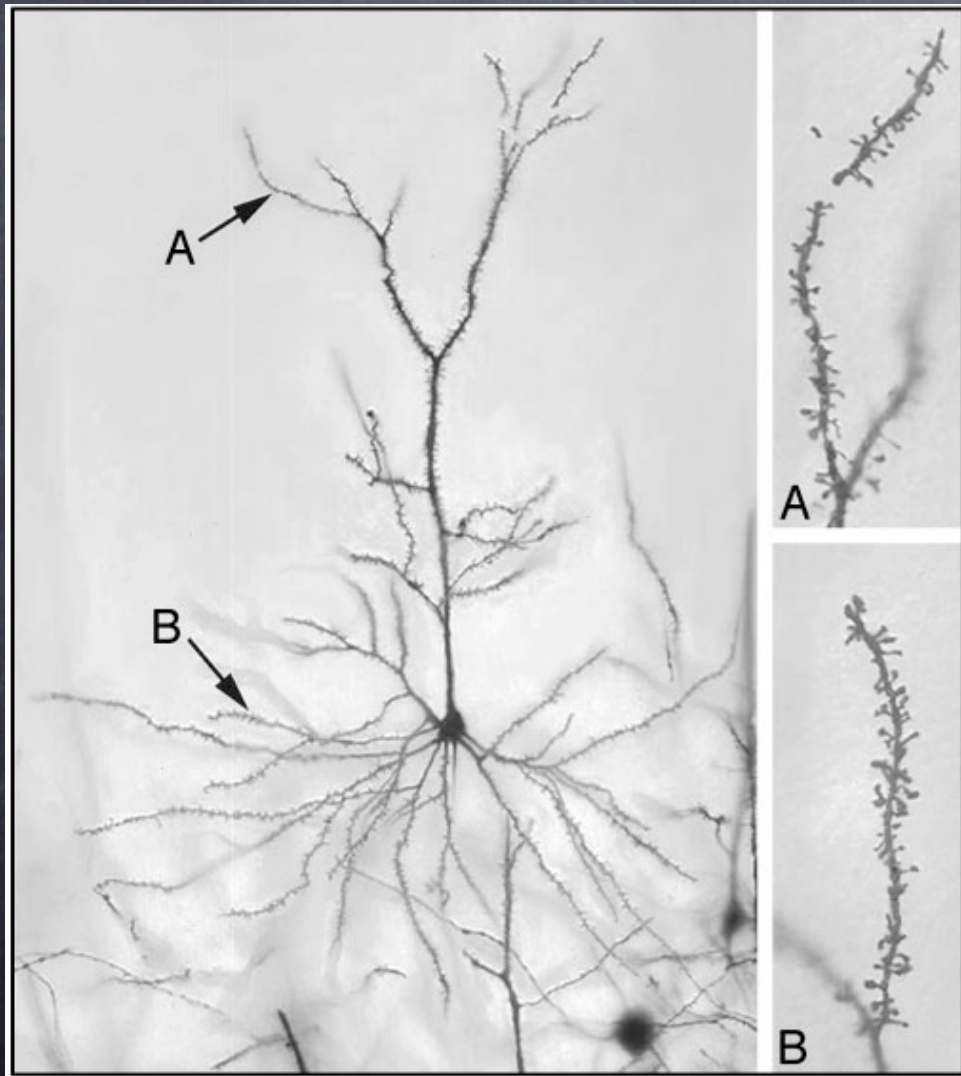
オレキシンの低下?

注意欠陥多動性障害

- Attention-Deficient Hyperactive Disorder
- methylphenidate (リタリン®) による治療

Amphetamine or cocaine limits the ability of later experience to promote structural plasticity in the neocortex and nucleus accumbens

B. Kolb et al. 2003 PNAS vol.100, 10523-10528



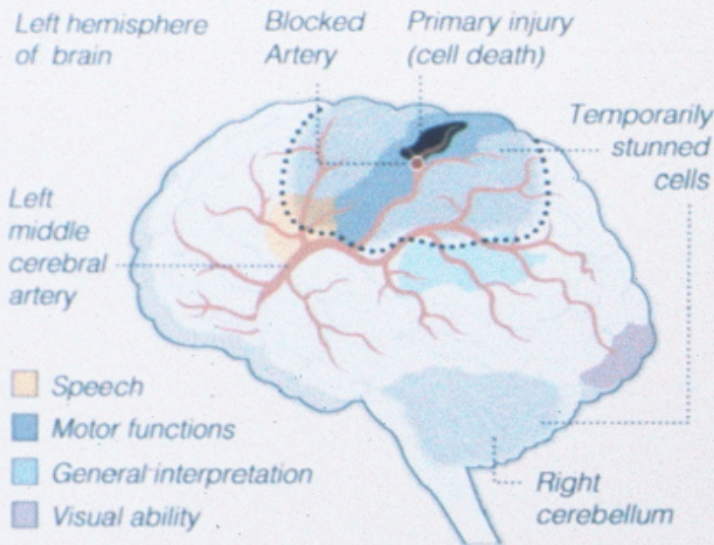
A combination of amphetamines and physical therapy

Repairing the Brain After A Stroke

A combination of amphetamines and physical therapy given soon after a stroke appear to accelerate recovery in patients.

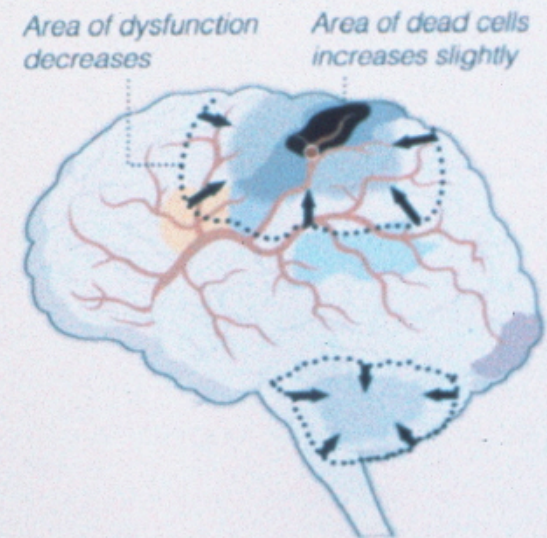
The Stroke

A stroke occurs when blood flow in the brain is blocked or an artery ruptures killing cells in a particular area. Surrounding cells are stunned, unable to perform their function. Additional areas connected to the injured region stop working when they cannot receive their input.



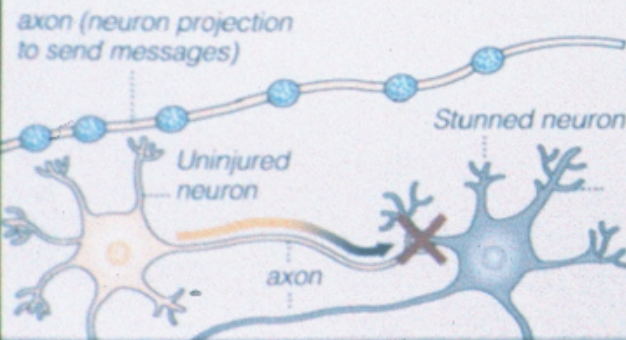
The Treatment

With the help of amphetamines and physical therapy the area of dysfunction can be reduced over time. Some of the cells die, but many others make new connections and start functioning, improving the patient's ability to move and talk.

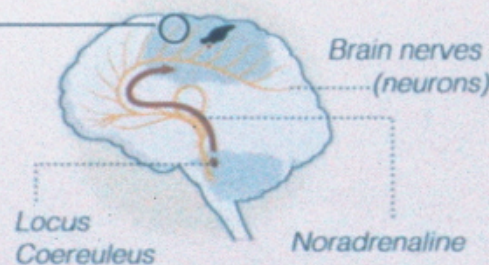


How It Works

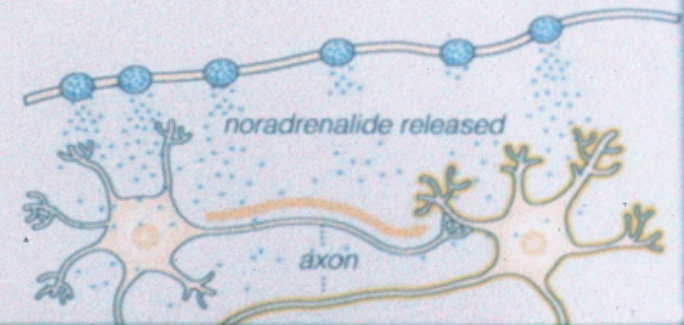
1 After a stroke, stunned cells cannot receive messages.



2 Amphetamines cause the release of noradrenaline stored in long neuron axons coming from the base of the brain...



3 ... flooding neurons and improving communication between them.

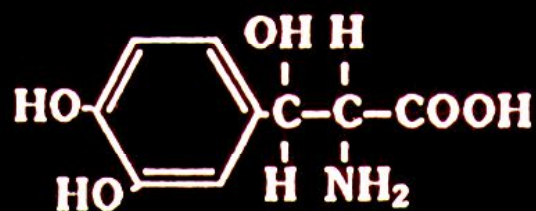


Effects of amphetamines

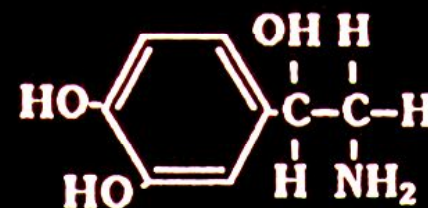
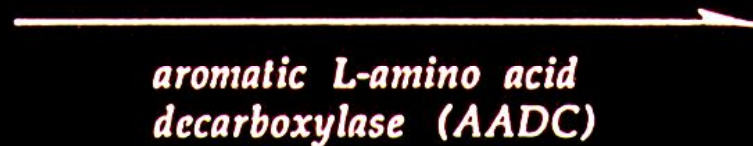


ドプス：ノルアドレナリン前駆アミノ酸

L-threo-DOPS is decarboxylated by AADC to yield *l*-norepinephrine



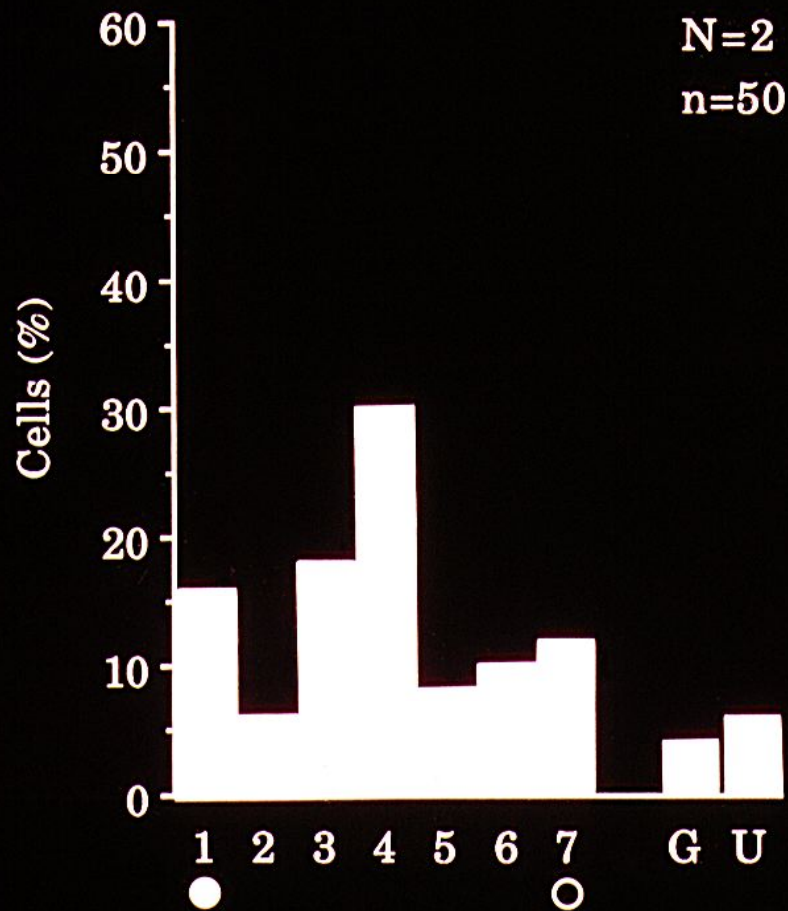
L-threo-3,4-dihydroxyphenylserine
(L-threo-DOPS)



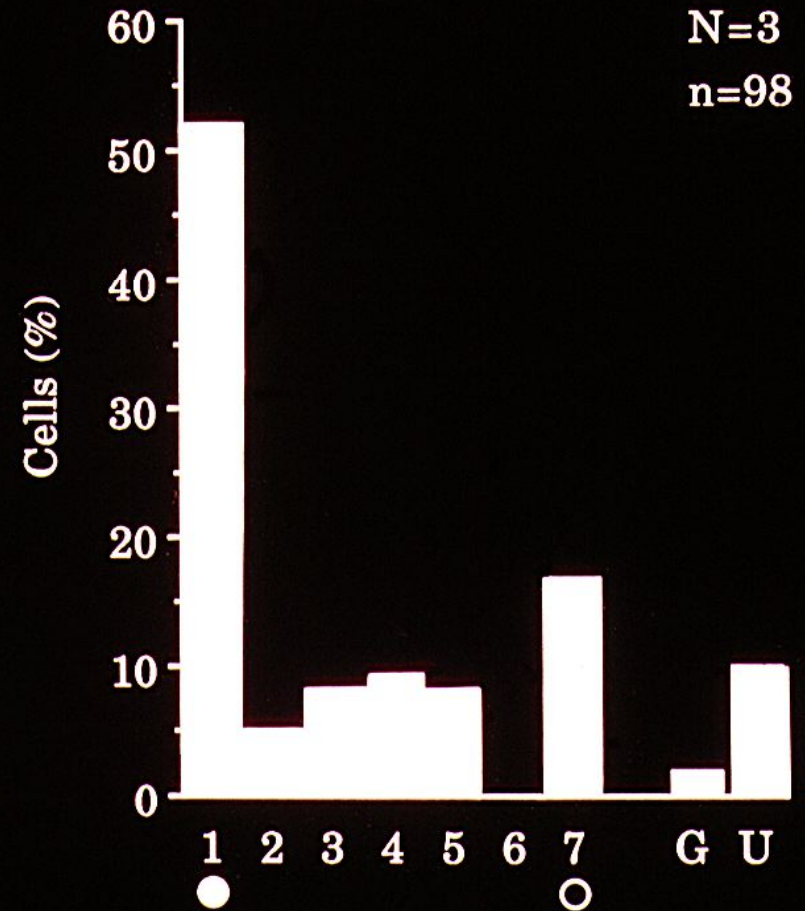
l-norepinephrine

L-DOPSによる成ネコでの 眼優位可塑性の誘導

A. MD



B. MD + L-threo-DOPS



CASE HISTORY

- Patient: I.I. 48 ys. old right handed male
- Stroke: 4 years ago, cerebral infarction in left parietal-temporal regions (include Broca's area)
- Status: right hemiparesis, motor aphasia
- Course: he admitted to the hospital to have speech therapy for several times without any improvement.

First admission : ST&PT therapy for 6 months

SLTA ; from 19/220 to 27/220, severe motor aphasia

Second admission : ST&PT therapy for 6 months

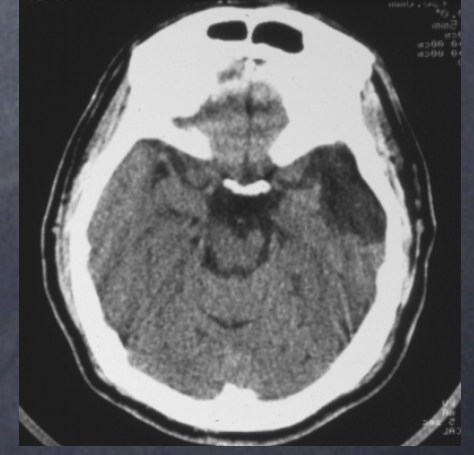
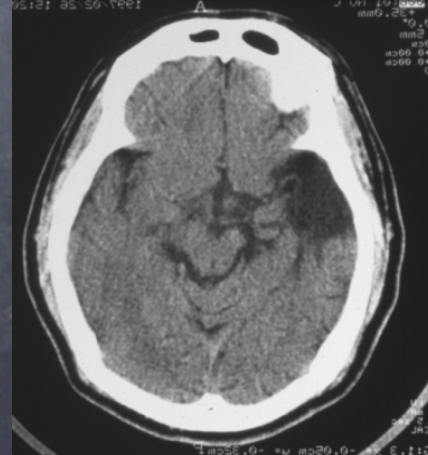
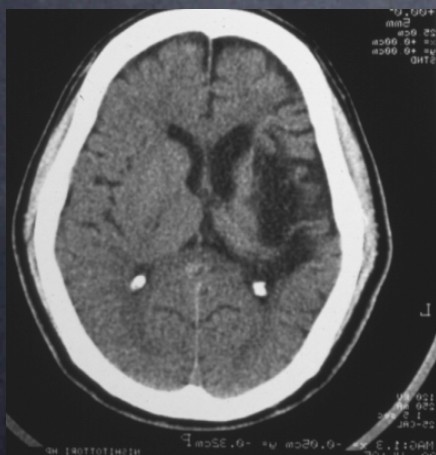
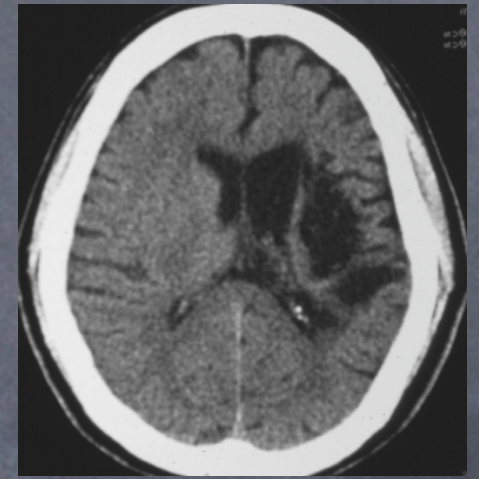
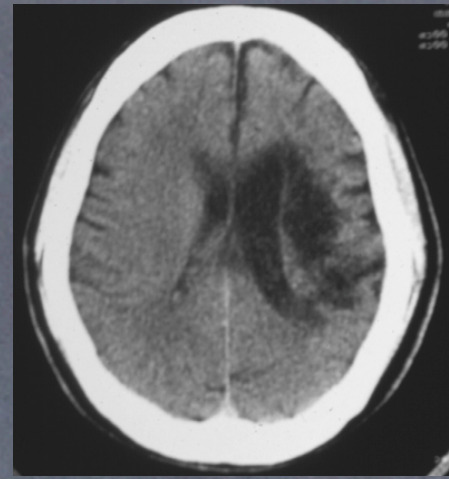
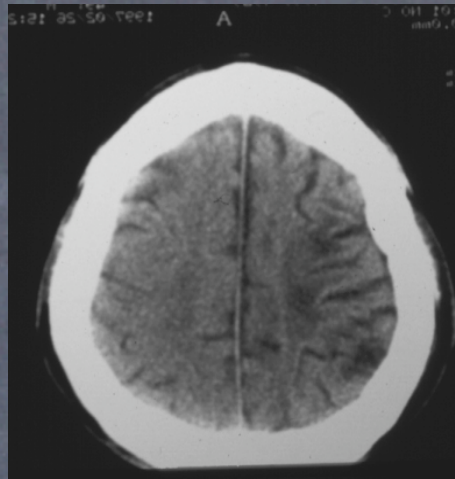
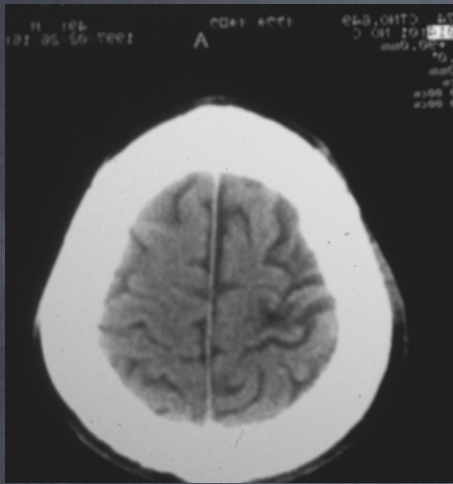
SLTA ; from 46/220 to 54/220, severe motor aphasia

Third admission : DX/ST&PT therapy for 6 months

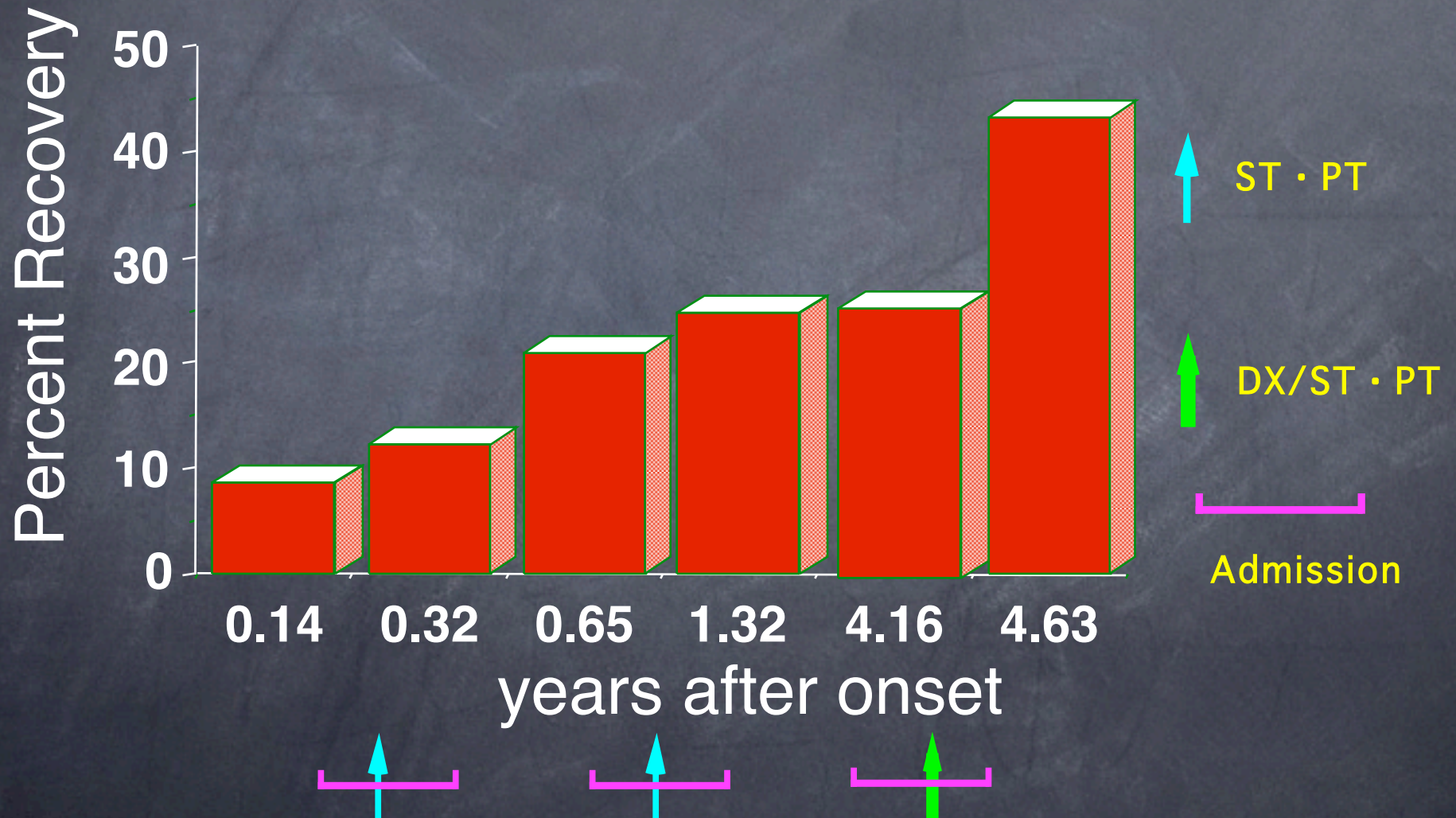
SLTA ; from 56/220 to 95/220, prominent improvement

moderate motor aphasia

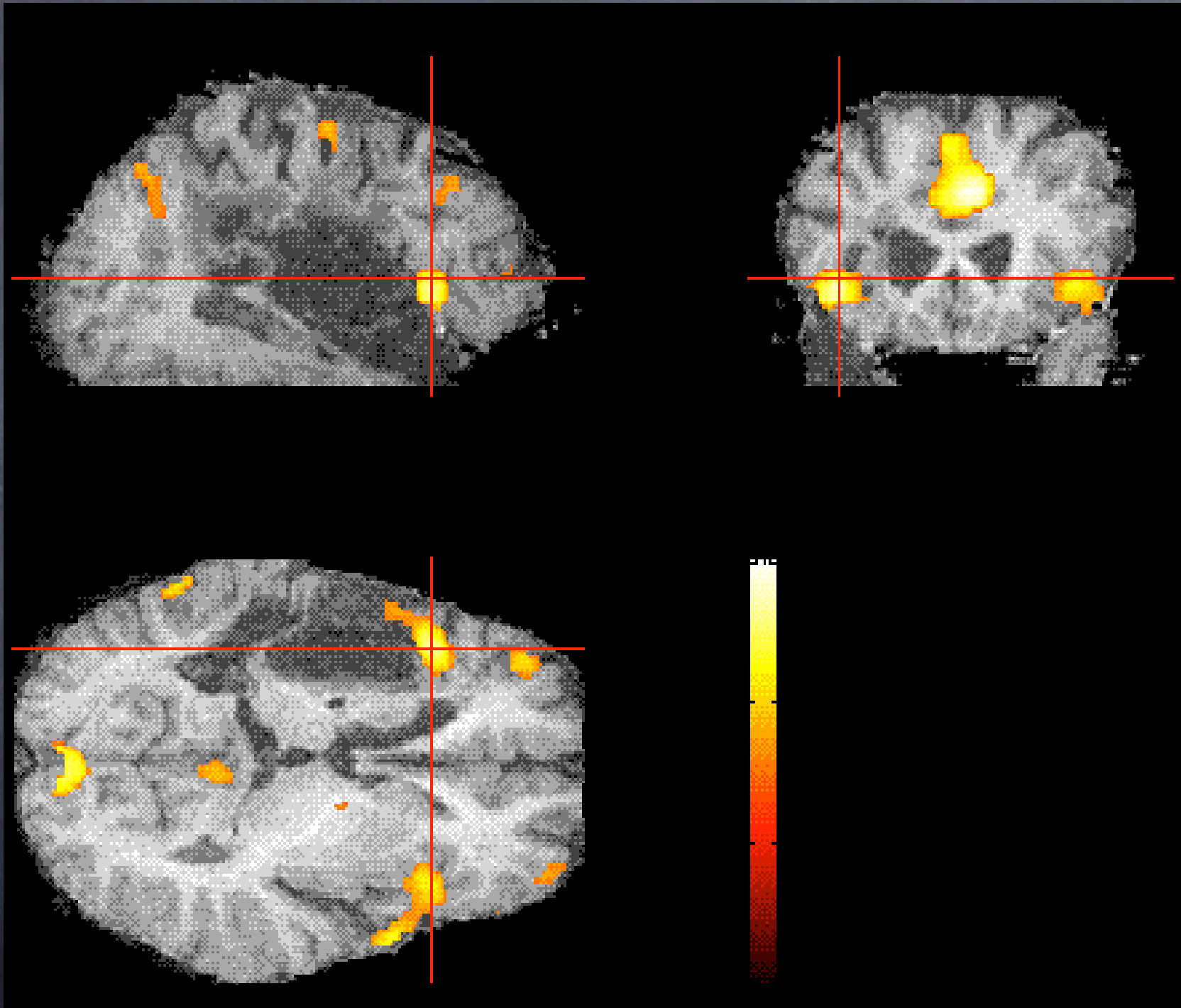
Brain Plain CT



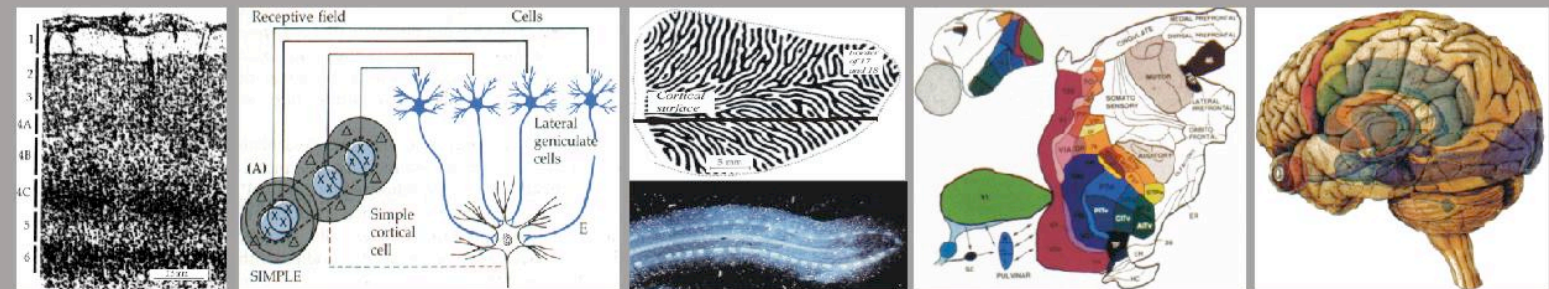
Temporal change of SLTA(%)



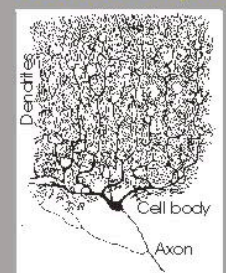
Activated Areas of fMRI by Covert Word Generation



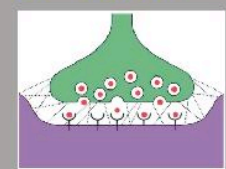
Spatio-Temporal Resolution of a Variety of Methods used in Neuroscience Research



D Cortical Layers E Circuit F Cortical Column G Cortical Map H Brain



C Neuron



B Synapse



A Molecule

