### 群馬大行動科学講義 脳の薬理学3



@標準藥理学 第6版 監修 康取 信 編集 今井 正 宫本 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.



# けいれん薬 convulsants

# picrotoxin pentylenetetrazol strychinin

# 蘇生薬 analeptic, 呼吸促進薬respiratory stimululants

### ø doxapram



●リゼルグ酸エチルアミド LSD 5HT<sub>1A,1C</sub> アゴニスト @フェンサイクリジン PCP NMDA antagonist © マリファナ marihjuana ● 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

Image: Advantage in the second se

synthetic cannabinoids; WIN55,212-2, ACEA, JWH-015

cannabinoids reduced microglial activation, MHCII antigen expression, CD4+ infiltrating T cells







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

Cannabinoids

Arévalo-Martin A. et al. 2003

# Methlxanthine系薬

### 誘導体 caffeine, theophyline, theobromine

◇ 細胞内Ca<sup>2+</sup>の動員 (0.5-1.0 mM)
 ◇ cAMP phosphodiesteraseの阻害 (> 5 0 mM)
 ◇ Adenosine受容体の拮抗 (<50 mM)</li>

Compelling Insight Into the Connection Between Caffeine and the Brain

### Coffee, Tea, Chocolate and the Brain

Edited by ASTRID NEHLIG INSERM, STRAUSBOURG, FRANCE

A volume in the Nutrition, Brain and Behavior series Chandan Prasad Louisuwa Store University, Baton Rouge, USA

TE1650 FL

#### A CLOSER LOOK AT CAFFEINE'S HELPFUL AND HARMFUL EFFECTS

NEW!

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

#### C O N T E N T S

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 Monicque M. Lorist

- 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, Monicque M. Lorist, 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. Lovallo
- 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



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
 methylphenidate
 ADHD

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.

Left hemisphere of brain

Left

middle

artery

cerebral

Speech

Motor functions

Visual ability .

General interpretation

#### Blocked Artery

#### Primary injury

#### (cell death)

Temporarily stunned

Right

cerebellum

#### The Treatment

With the help of anphetamines 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.

Area of dysfunction decreases

Area of dead cells increases slightly



### How It Works



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

cells



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



# How much brain is necessary for vison!

ANSVERSAL 26 TIME 5:16 4 \$ 256 A 1 SE/M SE 2013 20 1/2 220 VC 4K 6 0 0.6 .ICE 8 19 AT 74 RAN 15 4 R HGLE LR -12



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



# 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





### Modification of the Visual Cortex by Experience





#### Polar histogram of optimal orientations

Blakemore and Cooper, 1970

# A Reexamination of the Modification of Orientation Selectivity

Horizontal





V-6





Vertical







### MP Stryker and H Sherk 1975



Sengpiel, F et al. 1999

# Recording of the optical intrinsic signals by CAPOS



# Intirinsic Signals (Responsive areas become darker)



# Imaging Region of Interest



Illumination wave length: 700 nm

Visual stimulation: square-wave grating (S.F.; 0.5 or 0.15 Hz)

### Over-Representation of Experienced Orientation in Orientation Polar Map (v-Goggles)

Kitten B: PND 36 (2-weeks v-goggle reared)

Low SP



# Minimum Responsive Fields in the VC of Kitten Reared with v-Goggles



# Orientation Histogram Constructed by Unit-Recordings



# Function of an immediate early gene, c-fos



# Induction of c-fos mRNA following Visual Activation



### Noradrenaline-dependent Expression of c-Fos



Y. Yamada et al. 1999

## Ocular Dominance Patches Revealed by c-Fos Immunoreactivity Mapping



### Increase in c-Fos I.R. by the Goggle Rearing





### Oreintation Maps found in the Visual Cortex of Hydrocephalic Cat



# Summary

Our method with cylindrical-lens fitted goggles stably induces the overrepresentation of exposed orientation. This represent a step on the way to study molecular and celluar mechanisms of the "Orientation Plasticity".

An animal model for meridional amblyopia has been established.

# Thank you for your kind attention !