Behavioral and electrophysiological study on neural mechanisms underlying sensory recognition, emotional integration and behavioral expression: neurobiological basis of brain-inspired technology

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Abstracts-

To develop brain-inspired technology, neural mechanisms of perception, decision making and behavioral expression has been studied using animal models. The neural processes of these higher brain functions are under the strong influence of physiological and emotional conditions. In the present study, we demonstrate three neurobiological approaches to contribute brain-inspired technology: i) visual processing of texture and color recognition in the monkey, ii) chemical impacts on emotional processes in monkeys and rodents and iii) neural mechanisms of avoidance behavior in the frog. We found the texture specific neuronal responses which tuned to the density and element size, and sensitive to change in the orientation of shading by 180 degrees, in area V4 and the representation of color by hue and saturation in area V1 cortex. We also found reward-related neurons sensitive to catecholamines in the monkey orbitofrontal cortex, amygdala and lateral hypothalamic area. Chatecholamine systems are regulated by cytokines in stress condition and environmental chemicals during development. The putative collision-sensitive neurons of the frog are mainly located close to the tectal region corresponding to the focus of expansion of retinal images in the retinotectal map. These findings may provide useful insights to design new electrochemical devices which mimic neurobiological functions.

I. General Introduction

Adaptive neural mechanisms of perception, decision making and behavioral expression are under the strong influence of physiological and emotional conditions. To develop brain-inspired technology, we need to elucidate brain mechanisms of integrative adaptive processes using useful experimental models with optimal animal brains. In the present study we introduce several animal experiments using monkeys, rodents and frog to elucidate neural adaptive mechanism from perception to behavioral expression.

II. Visual recognition - psychophysical, physiological and theoretical study -

A. Introduction

One of our research units is destined to understand the mechanisms of visual information processing in the brain. The core fields are psychophysical study that measures visual perception psychologically and physiological study that records neural electric activities working for vision. To bridge from these fields to image processing and electronic devices that operate as the visual system of machines and robots, we also do some theoretical study.

B. Visual texture

Visual images consist of edges and textures. Edges exist at the boundaries of objects. Textures provide information about the material and friction of object surfaces. In the field of physiology, edges have been intensively studied in various visual areas whereas textures have not. A difficulty to study on texture is distinction between spatial frequency filtering and texture tuning. When the parameter of texture such as density and element size changes, spatial frequency of the image changes simultaneously. To avoid this confusion, we used textures consisting of small shadings. When the orientation of shading is changed by 180 degrees, the spatial frequency does not change (Fig. 1). On the other hand, perceived three dimensionality from shading or the direction of illumination becomes opposite. We recorded single neural responses to the texture stimuli in area V4 of macaque moneys. In area V4, there were neurons that showed texture specific responses, tuned to the density and element size, and sensitive to change in the orientation of shading by 180 degrees (Fig. 2,3). This tuning cannot be explained by that of simple or complex cells tuned to spatial frequency. We found the representation of visual texture in area V4, and the property of the cells can be modeled as a summation of outputs from local orientation detectors that have surround suppression [1].

C. Color

The information of color is represented as a point in a three dimensional coordinate system. This coordinate system starts as cone space that consists of the response amplitudes of long-wave, middle-wave and short-wave sensitive photoreceptors (cones), and is supposed to end in a coordinate system corresponding to color perception described by hue, saturation, and luminance. To find the representation of color in the brain corresponding to the perception, we recorded single neural activities in monkey LGN (a structure between the retina and the cerebral cortex) and V1 (where visual information arrives first in the cerebral cortex). The property of cell responses in LGN corresponded to the simple summation of retinal cone activities and did not correspond to the perception. Some V1 cells also showed stimulus selectivity similar to that of LGN. Others, however, showed selectivity for hue and saturation corresponding to the perception of color. We found that the representation of color by hue and saturation is achieved in area V1. This tuning to the hue and saturation of color can be modeled by simple neural network whose input-output function has sigmoidal nonlinearity [2]

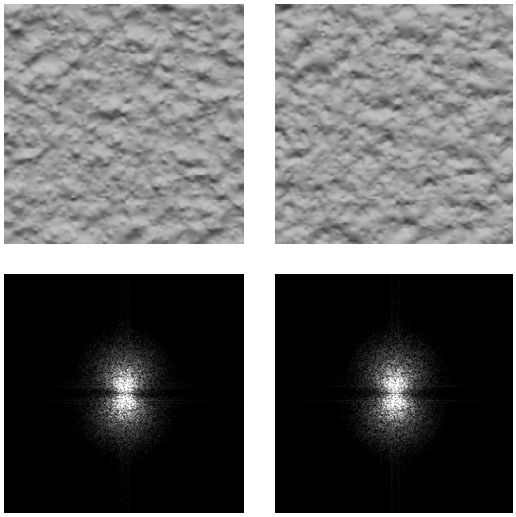

Fig 1. Two textures that consist of the same small 3-D structures and opposite lighting directions have almost the same Fourier power spectrum.

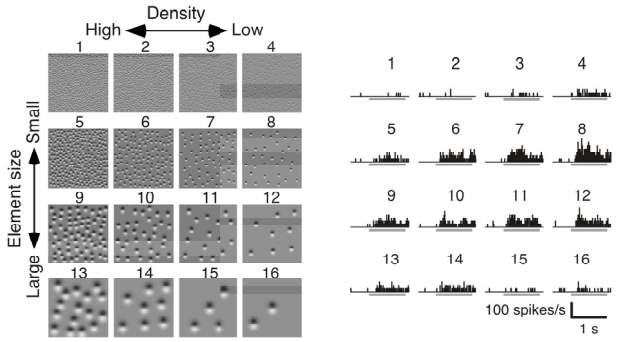

Fig 2. Neuronal responses of a representative cell selective for the density and size of the elements. This cell responded maximally to the stimulus of No. 12. Cells sensitive to spatial frequency, however, may exhibit similar tuning to the same stimulus set because each stimulus has unique Fourier power spectrum.

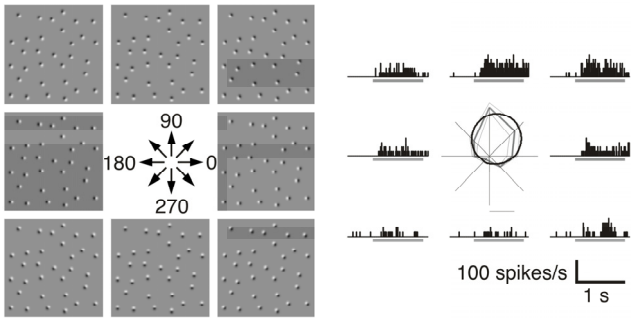

Fig 3. The same cell as in Fig. 2 exhibited selectivity for the orientation of the texture element. Note that this cell responded maximally to the stimulus of 90-degree orientation but did not responded to the stimulus of 270-degree orientation.

III. Chemical impacts on emotional integration

A. Introduction

Second research unit is destined to understand the mechanisms of emotional processing in the brain. The core fields are behavioral studies that analyze effects of environmental changes on different kinds of behaviors and and physiological study that records neuronal activities related to emotional control.

Brain mechanisms regulating behaviors and physiological functions are under the influence of chemical environments. Endogenous hormones, neurotransmitters and cytokines play important roles to maintain brain homeostasis. Environmental chemicals such as endocrine disrupters may also affect this process especially at the critical period during development.

Catecholamines, norepinephrine (NE) and dopamine (DA), regulate many different brain functions including learning and memory, emotion, stress responses and homeostatic control of physiological systems [3-6]. NE cells send their fibers to all over the central nervous system from cerebral cortex to spinal cord and DA cells to cortex, limbic system, basal ganglia and forebrain as the central autonomic system.

In this study, we demonstrate the functional linkage of catecholamines, cytokines, and environmental estrogenic compounds in the mammalian brain.

B. Chemical modulation of reward-related process in the monkey brain

Reward-related neuronal activity and its regulation by catechoamines were investigated in the orbitofrontal cortex, amygdala and hypothalamus of behaving monkeys by means of extracellular unit recording and microiontophoretic application of drugs [3-5].

Macaque monkeys (4-6Kg) were used for unit recording studies. Experimental procedures have been published previously [3-5]. The monkeys were trained to a high-fixed-ratio schedule consisting of (1) cue light to signal the start of bar pressing, (2) a high-fixed-ration bar-press task (FR20), (3) presentation of a short cue tone followed by a food reward, and (4) ingestion of the food (reward). Elecrophoretic application of chemicals and extracellular single-neuron recording were through a conventional multibarrel pipette.

Neuronal activity was modulated by reward situations and catecholamines. Activation of NEb receptors decreased, but that of NEα and DA D_2 receptors increased neuron activities during acquisition and/or consumption of rewards. The results suggest that NE and DA are differently involved in reward-related neuronal activity (see Fig 4).

C. Cytokines and monoamines in stress condition

Restraint stress as well as inflammatory stress stimulate NE release and enhance expression of interleukin-1β mRNA in the brain. A local injection of interleukin-1β induced an elevation of NE concentration in the medial prefrontal cortex [6].

Wistar rats were used for brain microdialysis to measure NE responding to local administration of interleukin-1β. The dialysate was analyzed for NE by using reverse-phase HPLC with electrochemical detection (Eicom, Kyoto, Japan).

IL-1-receptor antagonist and non-NMDA receptor antagonist blocked the effects of IL-1β. A cyclooxygenase inhibitor and a nitric oxide synthase inhibitor did not affect

the initial rise in NE levels observed 20 min after injection of IL-1β but completely blocked late phase of NE increase at 40 min and thereafter. These findings suggest NE system is locally regulated at terminal levels by cytokines in situation-dependent manner.

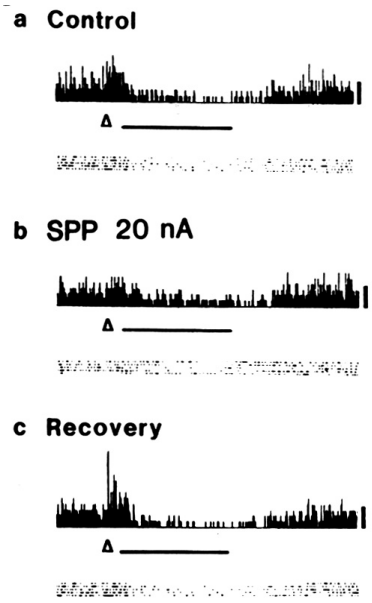

Fig. 4. Neuronal response to visual cue (triangle) signaling start of high-fixed ratio bar-press (under bar) task for food reward which was suppressed by iontophoteic application of spiperone (SPP), dopamine D2 blocker.

D. Developmental effects of environmental chemicals

The effect of exposure to estrogenic compound, bisphenol A (BPA), on the sexual differentiation of the NE system (the locus coeruleus) and related behaviors were examined in rats [7,8]. BPA was administered to mother rats during pregnancy and lactation at a dosage less than the tolerable daily intake level.

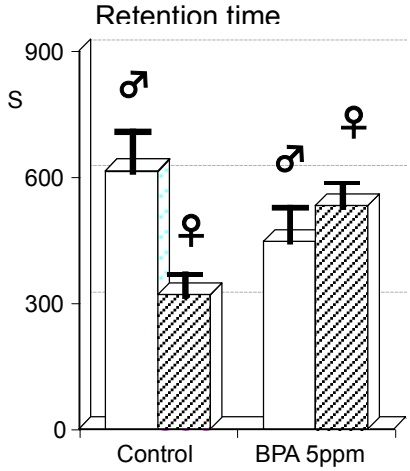

Fig. 5. Impairments of sexual differentiation of avoidance learning induced by early exposure of endocrine disrupters, bisphenol A during pregnancy and lactation periods.

Behavioral studies of Wistar rats exposing to bisphenol A were performed using a open-filed test and a passive avoidance test as previously described [7]. Volumes of locus coeruleus were calculated by the NIH image using magnified imale of Nissl-stained sections as previously described [7].

Control female offspring showed higher activity, grater stress coping, less avoidance learning and larger locus coeruleus than male controls, while the BPA-exposed group did not show any sexual dimorphism (Fig. 5,6). Our results suggest that the NE system is highly sensitive to endocrine disrupters during sexual differentiation in addition to cytokines.

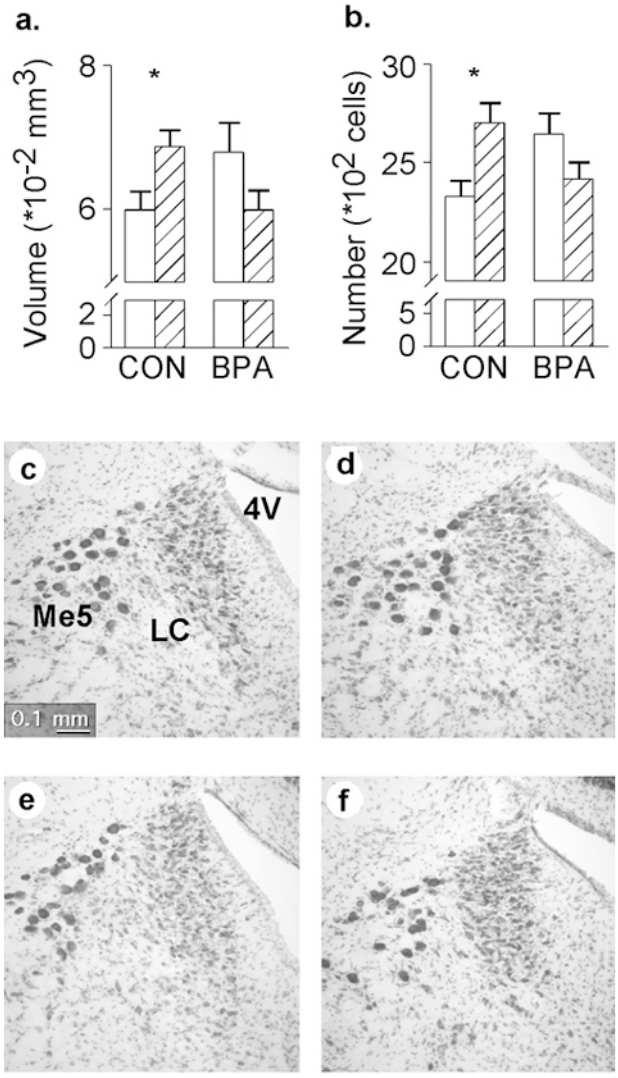

Fig. 6. Impairments of sexual differentiation of Locus coeruleus, noradrenaline neurons. Sex difference in the control group (male < female, c, d, respectively) was reversed in BPA group (male > female, e, f, respectively) [8]

E. Situation-dependent neural processing under the influence of chemical environments

The present study demonstrated that task-related activities of the cortex, limbic system and hypothalamus are strongly influenced by catecholamines originating from the brain stem. The catecholamine system have been reported to be involved in diverse adaptive functions including learning and emotion which is under the influence of other chemicals such as neuropeptides, hormones and environmental chemicals such

as endocrine disrupters [9,10]. Accumulating evidence also demonstrated that immunnological signals such as cytokines affects higher brain functions via catecholamines in particular situation such as inflammation or other stress conditions.

These multidimensional regulatory systems may provide new insight of neural computation models.

In conclusion, higher brain functions are under the control of catecholamines, cytokines and environmental chemicals.

IV. Behavioral expression: neural control mechanisms of avoidance behavior

A. Introduction

Third research unit is destined to understand the mechanisms of behavior control in the brain. The core fields are behavioral study that analyze avoidance behavior and physiological and morphological study that elucidates neural architecture working for behavior control.

The ability to avoid approaching objects on a collision course is essential for many animals to survive in the natural environment. To demonstrate input-output characteristics ofcollision avoidance behavior of the bullfrog, *Rana catesbeiana*, the behavior in response to visual stimuli simulating retinal images of objects approaching at two different constant velocities was examined. The analysis showed that the time difference between beginning of avoidance behavior and predicted collision was significantly larger for the object approaching at 2m/s than that approaching at 4m/s (Fig. 8). On the other hand, the threshold size of retinal images of approaching objects and maximum velocity of the avoidance behavior are not different significantly between the two stimuli. The results show that the essential cue of frog collision avoidance behavior is, as in the locust, size of retinal image rather than time-to-collision. The frog elicits collision avoidance behavior with fixed motion pattern when the retinal image of an approaching object reaches the threshold size, about 20 degree [11]. In recent study, we found that the frog could utilize depth information to control escape velocity during collision avoidance.

B. collision avoidance behavior

Based on a hypothesis that frog collision-sensitive neurons are in the optic tectum where obvious map of visual world is represented, we searched for the neurons by using a microelectrode array (5 by 5) in the left optic tectum of the anesthetized animals. We found that some tectal neurons give the strongest responses to objects approaching on a direct collision course through a path of 5 m, but no preference for objects approaching on a collision course over those approaching on deviated trajectories through a path of 1m. The putative collision-sensitive neurons are mainly located close to the tectal region corresponding to the focus of expansion of retinal images in the retinotectal map [12].

With multi-electrode and single-electrode methods, response property of putative collision-sensitive neurons (n=56) were further examined by using computer graphics to model looming stimuli. These collision sensitive neurons had smaller receptive field (RF) than those reported in the pigeon and the locust, and they were not activated with a looming object unless the focus of expansion of the image was located at the center of RF. Maximum response activity occurred when the approaching object had reached a specific visual angle ($q = 14.6^{o} \pm 3.4^{o}$, n=16), which is identical with the behavioral data. Thus, we propose that these neurons tell the animal the time at which visual angle of an approaching object reaches a specific value.

C. From neurobiology to robotics

Collision avoidance behavior includes detection of an approaching object and generation of adaptive escape jumping behavior to the imminent danger. Generally, with the present digital computer, visual information processing of natural scenes needs an enormous amount of calculation. Furthermore, it is impossible to detect and track a moving object in three-dimensional ever-changing real world with the present technology of image processing. Unfortunately, no robot can judge the dangers of an approaching object and generate adaptive escape behavior quickly at the present time. To demonstrate the neuronal mechanisms underlying response property of collision sensitive neurons and those of an integration of size and depth information obtained from an approaching object should give insight into development of quite new artificial vision system for collision avoidance task. To clarify the neuronal mechanisms underlying control of escape velocity depending on the dangers of an approaching object should give new idea for the development of control system which realizes smooth movement of a moving robot as in the biological system, the animals.

V. General perspective

Precise understanding of adaptive neural mechanism provides us the insights of basic model of brain-inspired devices. We are now starting collaborative research to develop brain-inspired devises which enable us to evaluate behaviors, emotional expression, physiological and pathological markers elicited from animals and humans.

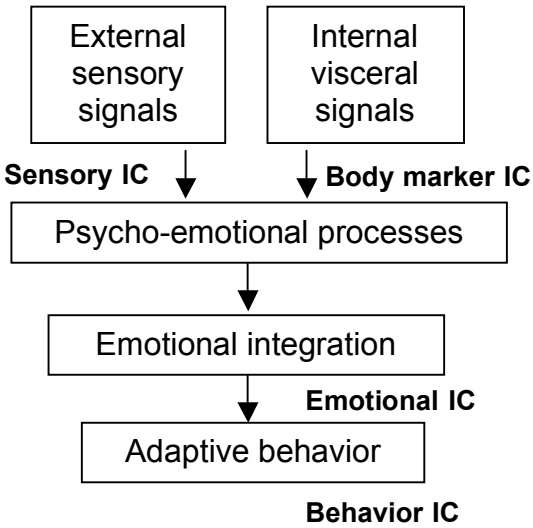

Fig. 7 Schematic diagram of basic neurobiological approach to brain-inspired technology.

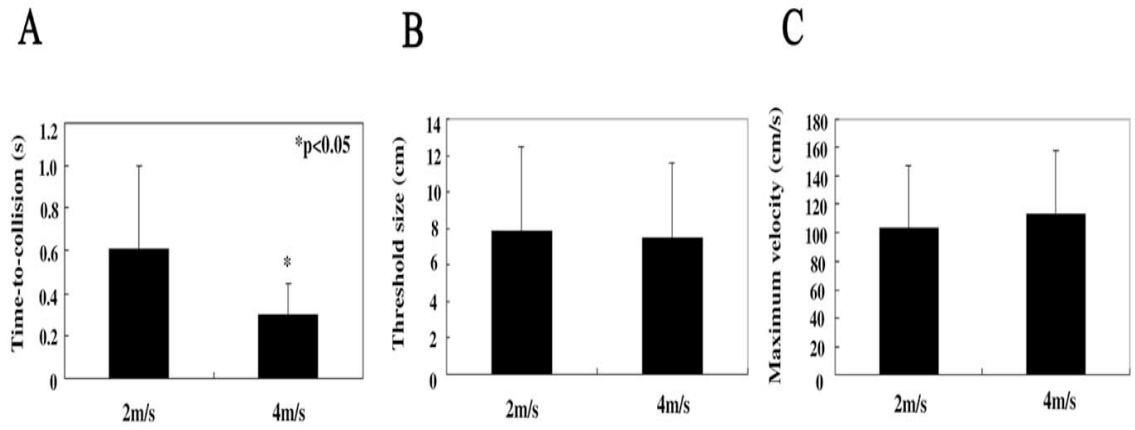

Fig. 8. A. Comparison between mean (± SD) time-to-collision of avoidance behavior to stimuli approaching at either 2 or 4 m/s. B. Comparison between mean (± SD) stimulus threshold size of avoidance behavior for stimuli approaching at either 2 or 4 m/s. C. Comparison between mean (± SD) maximum velocity of avoidance behavior to stimuli approaching at either 2 or 4 m/s. There is a significant difference ($p < 0.05$) between two stimuli only in time-to-collision. (modified from [11])

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