3-5 Visual Information and Eye Movement Control in Human Cerebral Cortex

KATO Makoto

Acquiring visual information such as reading a sentence, it is important to associate and visual image processing with an eye movement control. To elucidate mechanisms for processing brain information, it is necessary to make a functional map on a cerebral cortex in detail by measuring brain activity non-invasively using recently developed instruments. The present paper introduces a brain-mapping study to identify a functional region for eye movement control in the precentral area of the human cerebral cortex by using functional MRI. In this study, the eye movement regions were separated from the eye blinking regions, because both regions were activated during tasks conventionally used to examine the eye movement regions. Furthermore, problems about the functional mapping in the human brain are discussed with general problems in measurements for neuronal activity.

1 Introduction

While reading sentences such as this one, it is difficult for a subject to identify a character located only 10 characters away from the one on which the subject is currently focused. This is due to the fact that in the retina, our visual receptor, perception of visual characteristics is best at the center and diminishes exponentially when moving toward the periphery. In contrast, CCDs (charge-coupled devices) commonly used in video cameras do not show significant differences in visual characteristics—i.e., spatial resolution, color discrimination, and contrast dynamic range—between the central and peripheral parts of an image (Fig. 1). If the peripheral part of the retina were to function as effectively as the central area, the optic nerves projecting from the eyeballs would have to be impractically thick. It is suspected that as an adaptation to compensate for the low functioning of the peripheral portion of the retina, eye movement evolved to capture a continuous series of images with the central part of the retina through successive changes in focus. Thus, when acquiring visual information, as when reading sentences, cooperation between eye movement allowing a change in focus and the processing of visual information is essential.

With the human eye, spatial resolution, color discrimination, and contrast dynamic range diminish when moving toward the periphery of the visual field.

Invasive brain activity experiments performed in monkeys, the animals most closely related to humans, have revealed a considerable amount of information relating to the distinction between the area in the cerebral cortex involved in the control of eye movement and the area responsible for processing visual information.

Information on visual images captured by the retina is transmitted to the primary visual cortex of the cerebral cortex, which is located in the occipital lobe, via the optic nerve and

**Fig.1**   *Comparison of human eye and mechanical imaging*

the lateral geniculate nucleus of the thalamus. The information is then split and sent along two pathways: the ventral pathway toward the temporal cortex of the cerebral cortex, which primarily processes information on shape and color, and the dorsal pathway toward the parietal lobe of the cerebral cortex, which primarily processes information on characteristics such as motion, position, and size (Fig. 2).
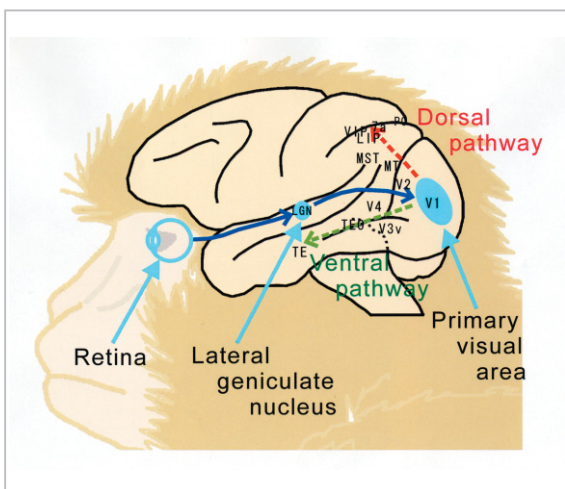

Fig.2   *Visual-processing pathway in monkeys*

The visual-processing pathway of monkeys is the most thoroughly studied site in the brain.

In the pathways related to the control of eye movement, the parietal eye field, located in the parietal lobe of the cerebral cortex, primarily handles positional information; it receives visual information from the visual areas of the occipital lobe, selects the target location to which the focus is to be moved, and finally sends the target positional information to the frontal eye field, located in the frontal lobe of the cerebral cortex. The frontal eye field is thought to convert the target information to information controlling eye movement and to send it to the midbrain (superior colliculus) and brain stem; therefore, it is the most important part of the cerebral cortex in terms of determining whether eye movement is carried out (Fig. 3).

The red areas show the input pathway and the light blue areas show the output pathway.

In the monkey frontal lobe, this frontal eye field is located in the anterior bank of the sulcus of the cerebral cortex, which is known as the arcuate sulcus. Electrical microstimulation is known to trigger eye movement, and recording of the electrical activity of neurons using microelectrodes shows transient activity both when the light spot is presented, which is indicative of eye movement, and during the
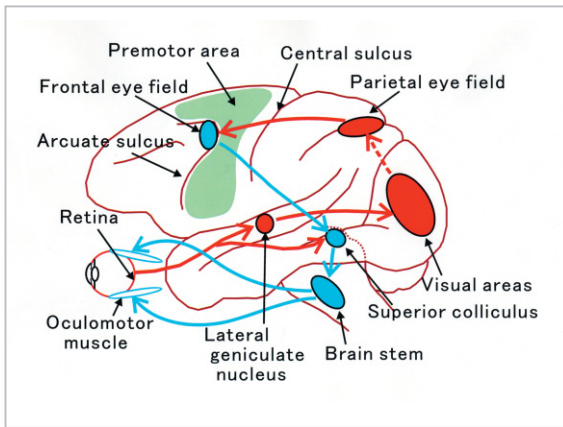
**Fig.3** *Eye-movement control pathway of monkeys*

eye movement itself [1]. In the region extending from the posterior bank of the arcuate sulcus to the anterior portion of the central sulcus (referred to as the "premotor area," adjacent to the frontal eye field), sites are also found in which eye movement can be induced by electrical stimulation, as well as sites in which neuronal activity associated with eye movement can be recorded [2][3]. Additionally, in these sites it is possible to observe hand and arm movement induced by electrical stimulation, which is not seen in the frontal eye field, or neuronal activity associated with hand and arm movement, suggesting that these sites are important in behavior requiring cooperation between hand and eye movements—as when pushing buttons, for example.

Thus, brain-function mapping in monkeys may be said to be quite advanced. On the other hand, in humans, a considerable amount of available information on the sites of the cerebral cortex that perform visual-information processing has been acquired through analogical inference from monkey studies, and in terms of the sites that regulate eye movement, the location corresponding to the frontal eye field identified in monkeys remains a subject of discussion.

2 Issues in human brain research

Two primary issues must be addressed when performing human brain research: the greater complexity, in comparison with mon-

keys, of the sulcus structure, which serves as a point of locational reference within the cerebral cortex, and the significant differences found among individuals (Fig. 4) [4].
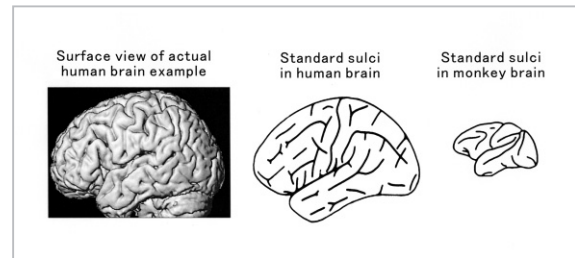

Fig.4 *Human cerebral sulci*

Only certain parts of the sulci are commonly seen in all humans. Most sulci vary from person to person, like fingerprints, and these structures are much more complex in humans than in monkeys.

In recent years, a method has been developed to create brain functional maps unaffected by individual differences, consisting of the merging of individual cerebral cortices, normalization of differences in size and appearance through three-dimensional image processing, and the averaging of data for a number of individuals (Fig. 5) [5].
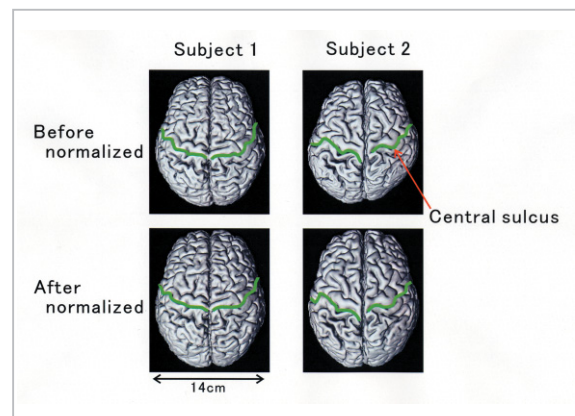
Fig.5 *Normalization of human brains*

The brain of subject 1 is relatively close in appearance to the normalized brain (standard brain), whereas the brain of subject 2 diverges considerably from the latter. Through normalization, the two brains become more similar in appearance, although the shapes of the sulci still show noticeable variations.
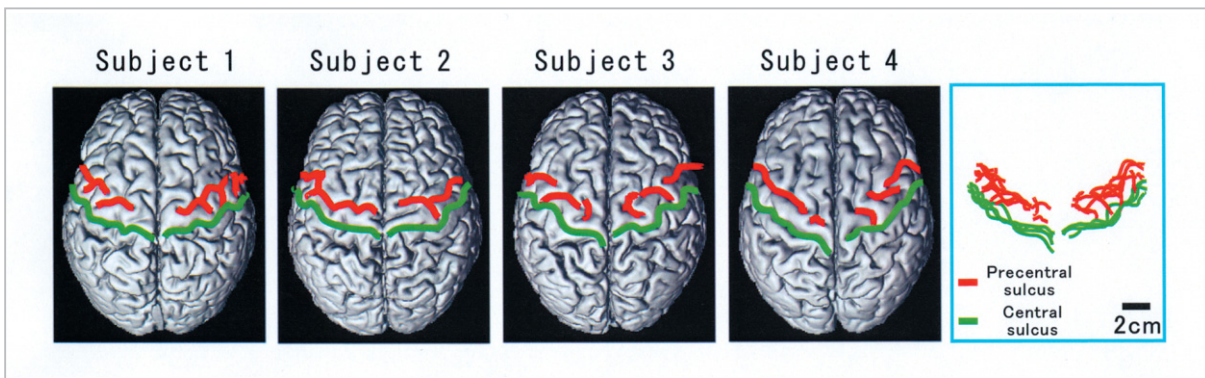
Fig.6 *Differences in representative sulci by subject*

The figure shows top views of the brains of four subjects compiled for the purpose of comparing their central and precentral sulci. The rightmost figure shows the overlapping areas of the sulci of the four subjects; deviations of 1 cm or greater by subject can be seen.

However, in the normalization process, rough appearance is regarded as important and information concerning sulci is virtually ignored. This can cause the position of a given sulcus to deviate by 1 cm or more from the normalized brain, depending on the individual, and often the site of the anterior bank of a particular sulcus in the brain of one individual may be located at the site of the posterior bank of the same sulcus in another individual (Fig. 6). Or the precentral sulcus, considered to be the location of the frontal eye field, could occur as one continuous sulcus in one individual and be divided into three parts or be bifurcated and connected to a posterior central sulcus, in another individual. On the other hand, if a brain-function map were laid out relative to the sulci, it is possible that functional areas smaller than 1 cm would not be detected after normalization.

Topologically speaking, the human cerebral cortex is a bilateral balloon-shaped organ, and research studies are conducted under the premise that the relative layout of the functional map does not depend on the individual. Although no reports based on the results of animal studies performed in mice, cats, or monkeys conflict with this premise, there is no guarantee that the premise holds true in the case of the human cerebral cortex, which has a vastly more complex shape. Thus, for the mapping of the human brain, which shows enormous individual variation in terms of shape, the creation of functional maps on an individual basis might require particular consideration in this regard, which is not the case with similar experiments performed in animals.

Another problem is encountered in determining the relationships between neuronal electrical activity and signals obtained through various methods of non-invasive brain activity measurement; as non-invasive brain activity measurement is a fairly recent development, these relationships have yet to be subject to sufficient analysis and thus remain as topics of ongoing study and discussion [6]. Primary non-invasive brain activity measurements currently in use include magnetoencephalogram systems, which detect electrical activity as magnetic changes; near-infrared measurement devices, which detect changes in oxy/deoxyhemoglobin concentrations accompanying electrical activity; and functional MRI (fMRI), which detects changes in magnetic susceptibility accompanying changes in oxy/deoxyhemoglobin concentrations. Information transmission between neurons occurs via sequential electrical pulses, referred to as action potentials, which essentially can be expressed in ones and zeroes (binary). Recording the action potentials of individual neurons is possible through the use of microelectrodes, an invasive method of brain activity measurement, and in fact neuronal information has

been analyzed using microelectrodes in animal experiments for many years. Magnetoencephalogram systems have the highest potential for detecting electrical activity, but even with these systems, whether the magnetoencephalograms are reflective of action potentials, synaptic currents occurring as neuronal input, or a mixture of both is dependent on the neuronal activity at the time of measurement and is therefore unclear. Changes in oxy/deoxyhemoglobin concentrations involve consumption of chemical energy by electrical activity, which is accompanied by increases in oxygen consumption and carbon dioxide concentration. Changes in the microvascular system of the brain resulting from this increase in carbon dioxide concentration trigger complex and multistep processes that render it difficult to distinguish the original changes in the electrical activity of neurons from changes in the signals detected by near-infrared measurement devices and functional MRI. Furthermore, limitations in the space-time resolution of these methods and living organism-specific noise (which greatly surpasses the physical noise inherent in the equipment) also present significant obstacles in human brain research. However, creation of a basic brain-function map using the currently available measurement methods remains an important task of human brain research, pending the development of future non-invasive brain activity measurement methods that can overcome the limitations of the measurement methods available today.
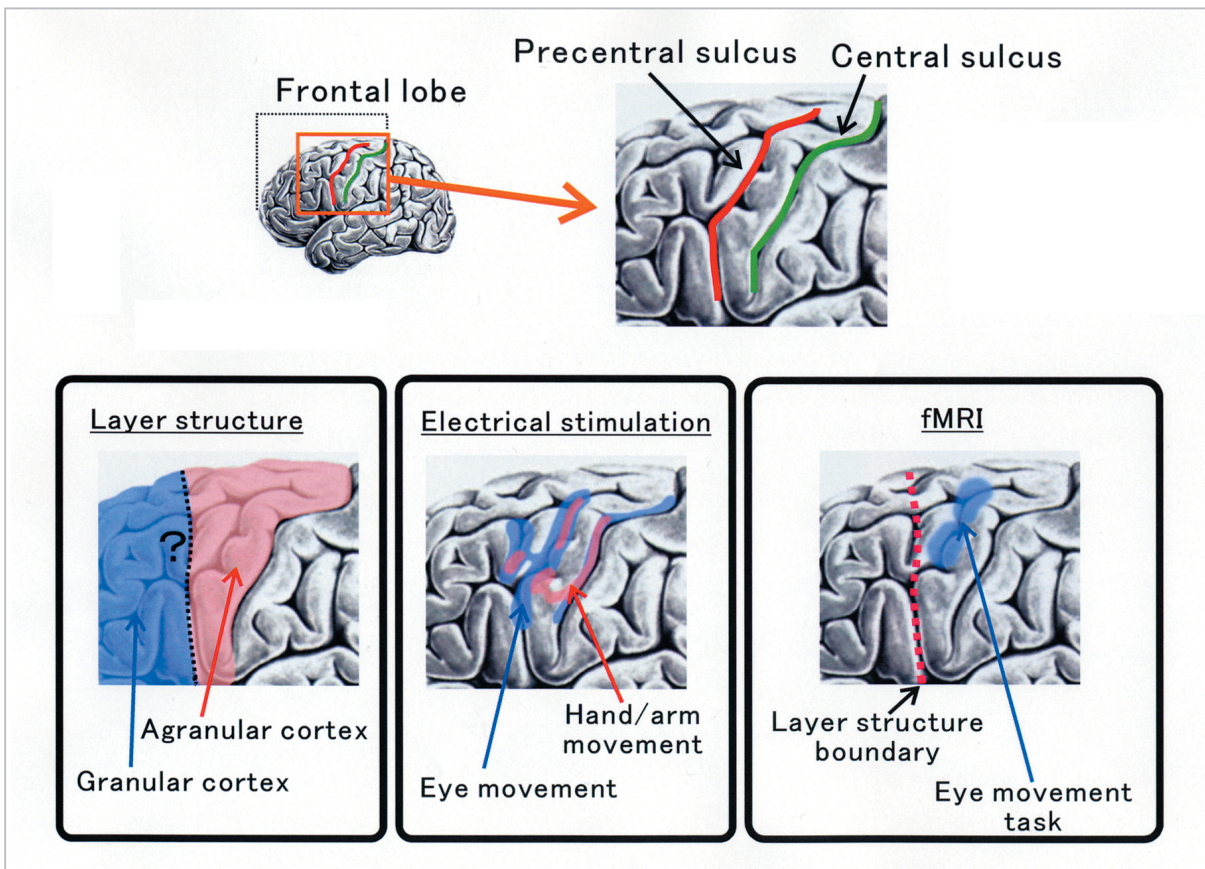
3 Where is the human frontal eye field that controls eye movement?

Given these circumstances, the question then becomes one of how to map the site in the human cerebral cortex that controls eye movement and corresponds to the frontal eye field identified in monkeys. Before non-invasive methods of brain activity measurement were not available, the human cerebral cortex had been searched for the frontal eye field identified in monkeys by comparing the histo-logical-layer structures of the cerebral cortices or by inducing eye movement via extradural electrical stimulation. In monkeys, in the layered structures, the frontal eye field is located near the boundary between the granular cortex and the agranular cortex. The analogous boundary in humans is significantly further anterior than the precentral sulcus. However, since the application of electrical stimulation induces eye movement over a wide area ranging from the anterior of the precentral sulcus to the anterior bank of the central sulcus, previously researchers were able only to localize the frontal eye field of humans as somewhere near the center of the posterior region of the frontal lobe (Fig. 7).

Layer structure comparison, electrical stimulation, and functional MRI produce different results.

Several reports on the use of functional MRI have been published since its establishment as a non-invasive method of brain activity measurement, given that performing eye movement is a relatively simple task [7]. Those reports indicated that during the execution of eye-movement tasks, the area near the anterior and posterior bank is activated by eye movement, along with the precentral sulcus. Since these results placed the frontal eye field at a position considerably more posterior than was estimated based on comparison of the histological-layer structures of the cerebral cortexes, it was suspected that the active region for blinking movement, which is inevitably a part of any eye-movement task, was mistakenly reported as the active region of eye movement [8]. In fact, individuals who perform an eye-movement task are often observed to blink unconsciously immediately after performing an intentional saccadic eye movement. Blinking movement is actually the same type of body movement as hand and foot movement, and it would not be considered strange if the site of blinking control were located in the posterior of the agranular cortex, a site far posterior to the boundary between the granular and agranular cortices. Accordingly, in the present study, sites related

Fig.7 *Past results of research performed in areas near the human frontal eye field*

to blinking movement that might be located within the site activated when an eye-movement task was performed were identified as a means of narrowing down the list of potential sites related to eye movement.

In the experiments, brain regions that are activated by eye movement excluding blinking movement were identified by having subjects perform four different tasks as described below and comparing the resultant brain activities.

(1) The subjects follow a light spot shown on a screen that moves to a new position at one-second intervals.

(2) First, the subjects fixate their eyes on a light spot that appears in the center of a screen. The spot disappears after one second to reappear in the periphery of the screen; the subjects then re-fixate on the spot. The second light spot disappears after 0.5 seconds and reappears in the center two seconds later. These steps are repeated.

(3) The word "BLINK" is shown in the center of a screen. While this word is visible, the subjects repeatedly blink at their own pace. The subjects are to keep their eyes as still as possible.

(4) The word "OPEN" is shown in the center of a screen. While this word is visible, the subjects are to refrain from blinking as much as possible. The subjects are to keep their eyes as still as possible.

The figure shows MRIs of subjects recorded while they performed eye-movement tasks. While blinking did not tend to occur with task 1, blinking (red vertical lines) did occur as subjects performed task 2.

Although tasks 1 and 2 are similar in that they both involve eye movement, it is known that blinking does not tend to occur immediately after eye movement during continuous eye movement as in task 1, in contrast to intermittent eye movement tasks such as task 2. Therefore, by comparing the brain activity occurring during tasks 1 and 2, it is possible to
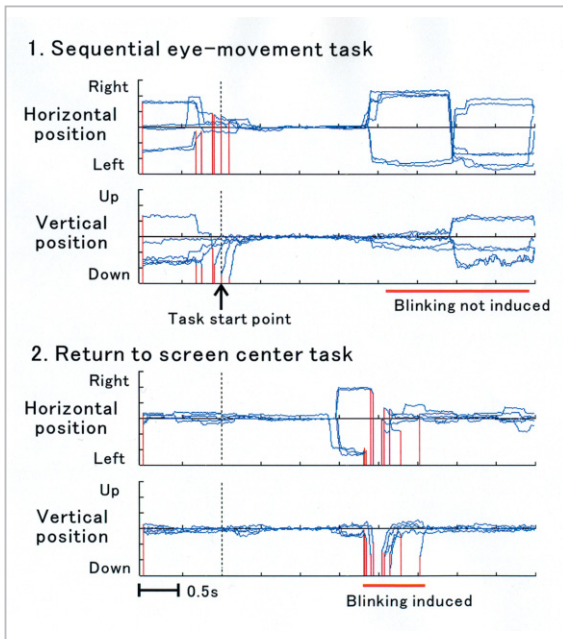
Fig.8 *Eye-movement traces*

determine the sites of the brain that are activated by blinking immediately after eye movement (Fig. 8). Task 3 was performed to permit the observation of sites of brain activity seen only with blinking. However, given the possibility of detecting brain activity associated with movement control resulting from the viewing of words, the results of the activity were compared with those of task 4, which was performed as a control in which subjects viewed words but did not perform blinking.

As a result, the most posterior region of the superior frontal sulcus, which is located within the regions activated during the eye-movement task near the anterior/posterior bank along with the precentral sulcus, was found to be activated by the eye-movement task but not by the blinking task. The immediately lateral (outside) areas were activated by both the eye-movement and blinking tasks (Fig. 9). The fact that no differences were seen between the brain regions activated by the eye movements performed in tasks 1 and 2 suggests that the brain activity induced by the blinking accompanying eye-movement tasks is negligible in comparison with that associated with eye movement. These data suggest that the frontal eye field of humans is located in the anterior/posterior bank along the precentral sulcus, which is near the most posterior part of the superior frontal sulcus, and is located considerably posterior to the putative site of the frontal eye field estimated by comparison of the histological-layer structures of monkeys and humans.

A brain site that is activated by eye movement but not by blinking (red area) is seen in
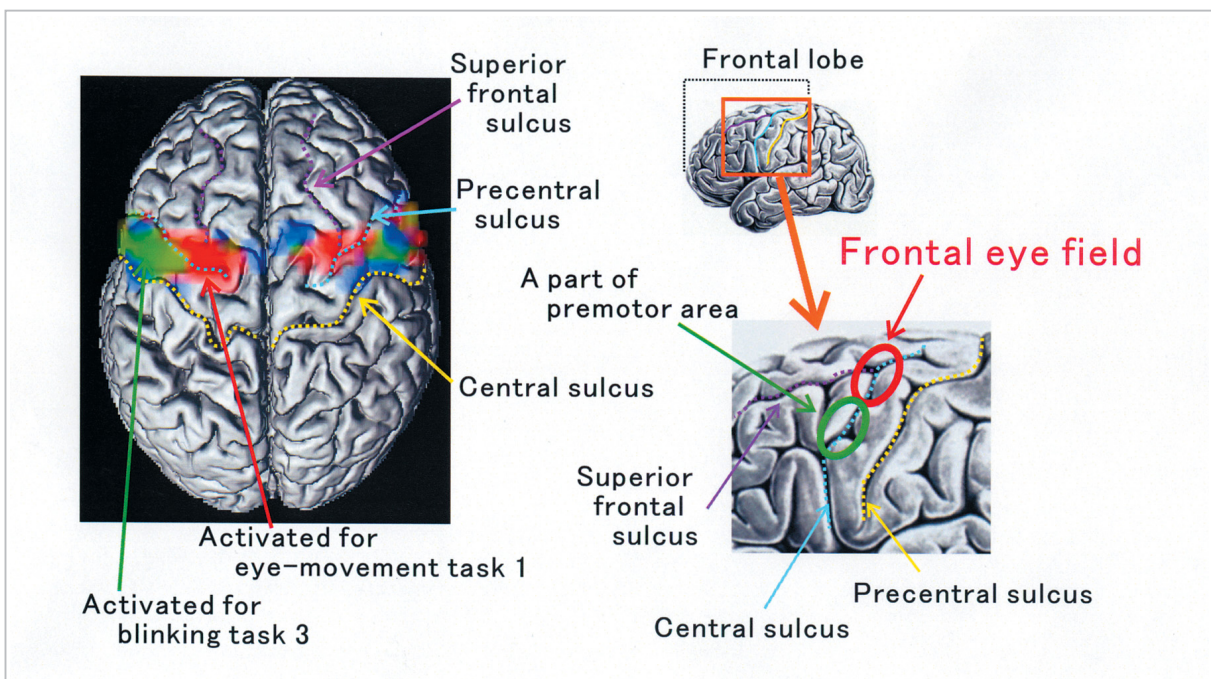
Fig.9 *Frontal eye field identified by functional MRI*

the medial part of the precentral sulcus, suggesting that this area is the frontal eye field of humans.

The brain likely requires less than 20 calculation steps to aim at a particular target. If we were to attempt to perform such calculations using sequential programming available today, at least thousands and possibly more than tens of thousands of calculations would be required. While the wavelength of the information handled by the neurons of the brain is only several hundred hertz, the brain can perform these calculations without difficulty in less than one second, as these calculations are performed by a massively parallel calculation mechanism that far exceeds our current technology and knowledge, and also because our mechanisms allow us to perform the programming required for such calculations automatically. If these mechanisms could be applied to current silicon technologies, which make use of operation frequency much higher than those found in brain activity, we might in fact attain the state sought after by those researchers working to improve clock frequency to nearly the limit of physical characteristics. This cannot be accomplished using current technology, but the application of the mechanisms in question could likely open a path toward this goal. However, the fact remains that while brain research to date may be able to answer questions as to where activity occurs, such research cannot answer questions as to how it occurs.

It is also true that in itself the massive parallelism of the brain hampers brain research. At present, the largest-scale example of observation and calculation of such massive parallelism is found in global weather observation and forecasting. Placing a mesh every 10 km over the Earth's 500-million-km^2 area would provide five million observation points. In the brain, the interval between neurons is approximately 50 μm; if the observation points are considered analogous to neurons, then (based on a cerebral cortex with a thickness of 3 mm) the interactions over the entire surface of the earth would only correspond to 2 cm^2 of neu-

ral brain interactions. Thus, while there is no comparison with the entire human cerebral cortex, which is known to be 1,600 cm^2, processing based on the corresponding number of neurons in the future is not out of the question. In fact, the frontal eye field alone may prove of manageable complexity and hence it might be possible to calculate the behavior of all neurons in the frontal eye field. However, in the case of neurons, signals from distant neurons through nerve fibers must be taken into account in addition to the interactions between mesh lattice points; the resultant limitless number of combinations poses yet another problem.

Furthermore, while it is possible to situate weather observation points at intervals to provide sufficient practical distance between each observation device, this does not apply in the case of brain-activity observations. The intervals between neurons are only 50 μm—only approximately 10 times the few μm of the tips of the microelectrodes used to record the activity of neurons. On the other hand, the diameter of the shaft of each electrode is a few hundred μm, therefore it would be impossible to deploy a great number of electrodes in close proximity. Still another issue arises in that weather observation devices automatically transmit an abundant amount of data (or, more accurately, they are designed to do so), whereas when recording the activity of neurons using current microelectrode-based technology, the observer must obtain recordings by making minute adjustments in the positions of the microelectrodes manually, with careful monitoring. This is because recording conditions change along with changes in heart rate, respiration, and blood pressure; consequently, even today, the number of simultaneously recordable neurons is fewer than 100, and we have managed to make practical use of only 10. If we are to observe massively parallel operations in which more than a few tens of thousands of neurons simultaneously work together to perform one-step calculations, the current sequential observation technologies—whether invasive or non-invasive—used to

monitor brain activity must advance far beyond current levels. Thus, today's brain researchers must first resolve the problem of the lack of technology available to observe such massive parallelism.

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KATO Makoto, *Ph.D.*

Senior Researcher, Brain Information Group, Kansai Advanced Research Center, Basic and Advanced Research Department

Neuroscience