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Functional Mapping of the Human Visual Cortex Using Electrical Cortical Stimulation and Flash Visual Evoked Potentials

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전기적 뇌자극과 광시각 유발전위 검사를 통한 인간의 시각 피질에서의 기능적 분화 양상

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- 국문초록 -

연구배경 및 목적 : 시각 인지 과정은 영장류 실험을 통하여 다소 정보를 얻을 수 있었으나 인간에서는 아직 완전하게 이해되지 않고 있다. 이 연구의 목적은 뇌자극과 시각유발전위 검사를 토대로 인간의 시각피질의 기능적 분화와 시간순으로 활성화되는 양상을 보고자 한 것이다. 연구방법 : 간질 수술을 위하여 후두엽과 인접 부위에 광범위하게 피질하전극을 넣은 22명의 환자를 대상으로 전기적 뇌자극과 시각유발전위 검사를 시행하였다. 뇌자극시 나타나는 반응은 형태, 색, 및 움직임의 세가지로 크게 나누고 형태는 다시 단순, 중간 및 복잡한 형태로 세분하였다. 시각유발전위는 P1 혹은 IV파의 latency를 측정하였다. **결과** : 단순 혹은 중간 형태는 흔히 occipital pole과 striate cortex에서 발생하였다. 색반응은 후두엽의 기저부 즉, fusiform, lingual, inferior occipital gyri를 자극할 때 관찰되었다. 움직임 반응은 내측기저부 및 외측의 측후두엽 혹은 측두정후두부의 경계부에서 주로 나타났다. **결론** : 이러한 결과는 인간의 시각피질이 시각의 여러가지 구성성분 즉, 형태, 색, 및 움직임에 대하여 각각 별도로 분화되어 있다는 것을 보여준다. 또한 시각자극이 전해지면 striate cortex와 occipital pole이 가장 먼저 활성화되고 이어서 내측 및 외측 후두엽 부위가 활성화된다는 것을 알 수 있다. 이러한 사실을 종합하여 보면 인간의 시각피질은 시각의 여러 구성성분별로 별도로 발달된 해부학적 경로를 통하여 각각의 기능에 대하여 특수하게 분화된 뇌세포에서 시각정보를 각각 분석하되 일정한 시간순서에 의한다는 것을 시사하는 것이다.

Key Words : Human visual cortex, Functional organization, Sequential activation, Electrical cortical stimulation, Visual evoked potentials

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INTRODUCTION

In vision, we experience the world as a whole. However, the process of visual perception has not been fully understood. Recently, we have thought that various and otherwise unrelated attributes - form, color, movement, and location etc. - are all coordinated in a visual image and that there are at least three different neural pathways in the brain[1].

In fact, the concept of functional organization or specialization in the visual cortex did not occur until the middle of the 20th century. It was usually based on studies of macaque monkey, which showed that, of many visual areas outside the striate cortex, one area (V5) is specialized for visual motion, while another area (V4) for color[2-4]. In human, based on clinical examination of patients with cortical lesions, there has been some suggestions that specific regions of extrastriate or association visual cortex may be specialized for form, color, and motion. There is an agnosia for form that can be selective for inanimate or animate objects, or for familiar faces only (prosopagnosia). Some patients lose color vision (achromatopsia) because of localized damage of the basal temporal cortex, who otherwise have reasonably good vision[5-7]. In addition, after a bilateral damage in the cortex of medial temporal or medial superior temporal cortex, movement agnosia, so-called cerebral motion blindness, may occur, which is manifested as a selective loss of movement perception without loss of any other perceptual capabilities[8-9]. It is more recent that the study for functional specialization in human visual cortex is available. Of these, Zeki[10] reported a positive functional relationship between the striate/peristriate cortex, the lingual/fusiform gyri during color vision and the striate/peristriate cortex, the temporo-parieto-occipital junction during motion stimulation by PET study.

With tremendous progress in epilepsy surgery, many methods for functional mapping have been developed, of which electrical cortical stimulation and evoked potentials can be done directly in human brain with subdural electrodes in epilepsy surgery patients. Cortical electrical stimulation recently has been performed routinely to map areas of specific brain functions, and it enables testing in greater details and over a longer period of time. Lesser et al.[11] demonstrated motor and sensory mapping of the frontal and occipital lobes using both intraoperative and extraoperative cortical stimulation. They reported a relationship between specific cortical regions and corresponding visual fields in 4 patients with visual cortex stimulation. In the same 4 patients, Arroyo[12] showed a pattern of sequential activation, that is, visual information is transmitted serially from the striate to the other parts of the visual cortex by comparing the latencies of patterned VEP waves. However, the precise functional localization and temporal distribution of human visual attributes have remained largely unclear.

In this study, we wanted to validate functional organization directly in the human visual cortex using electrical cortical stimulation and to demonstrate sequential activation of visual cortex by analysis of VEP waves.

METHODS

PATIENTS

Twenty-two epilepsy surgery patients were included, in whom invasive study was done with subdural electrodes over occipital and adjacent cortical areas. Twelve patients were females and ten were males. The ages of those patients ranged from 3 to 43 years (mean, 23 yr). All patients underwent the precise investigational procedures according to Samsung Medical Center Epilepsy Surgery Protocols including clinical examination, continuous video-EEG monitoring, brain imaging, invasive study, electrical cortical stimulation, evoked potentials, surgical procedures and pathological diagnosis. Pathological study showed cortical dysplasia (7/22), gliosis (6/22), hippocampal sclerosis (3/22), cavernous angioma (3/22), oligoastrocytoma (2/22), neurocysticercosis (1/22). At least, all results were obtained from cortical areas out-

Microsystems, Mountain View, Calif) in neuroimaging laboratory. Image processing consisted of three steps. The first step was MRI-CT registration and transformation. Cerebral area of MRI was segmented by autotracing and manual boundary limit decision. And corresponding CT area was segmented by manual tracing. Before registering between two images, brain structure of MRI and CT was segmented and saved in 16 bit gray scale image and one bit binary image. One bit CT image was transformed to MRI by chamfer surface matching algorithm. In this process, most suitable transformation matrix was made. The mean matching error was about 5 mm[15].

The second step was subdural EEG electrodes segmentation of transformed CT. By manually tracing, the subdural EEG electrodes appeared on transformed CT, Subdural EEG electrodes were segmented from 16 bit transformed CT and saved in 16 bit gray scale and one bit binary image.

The final step was multi-object rendering. Original MRI voxel size was 0.86×0.86×1.7 mm, so it had to be reconstructed isotropic voxel size (0.86×0.86×0.86 mm) to represent real brain size (Fig 1). Also Segmented subdural electrodes were reconstructed isotropic voxel size (0.86×0.86×0.86 mm). Voxel gradients transparency rendering method was used[15-16]

RESULTS

RESPONSES OF CORTICAL STIMULATION

Electrical cortical stimulation of the human occipital cortex produced various visual responses. As Penfield and Jasper[17] described in 1954, electrical stimulation on both the mesial and the lateral occipital cortex produced simple visual illusions. These sensations were mainly single spot of white or black light at a constant position in the visual field, although for some electrodes they were two or several such spots and the size ranged from tiny punctate sensations up to a large coin at arm' s length. These sensations of light were later called "phosphenes" by Brindley and Lewin[18]. Phosphenes usually disappeared immediately when stimulation ceased, but after strong stimulation they persisted long, sometimes up to 30 seconds. Stimulation of the posterior temporo-parieto-occipital junction elicited complex visual illusions, such as animal, face, body part or even landscape. These simple and complex illusions were sometimes associated with moving sensation. There were also color responses, both formed and unformed, sometimes showed one color, or multiple colors such

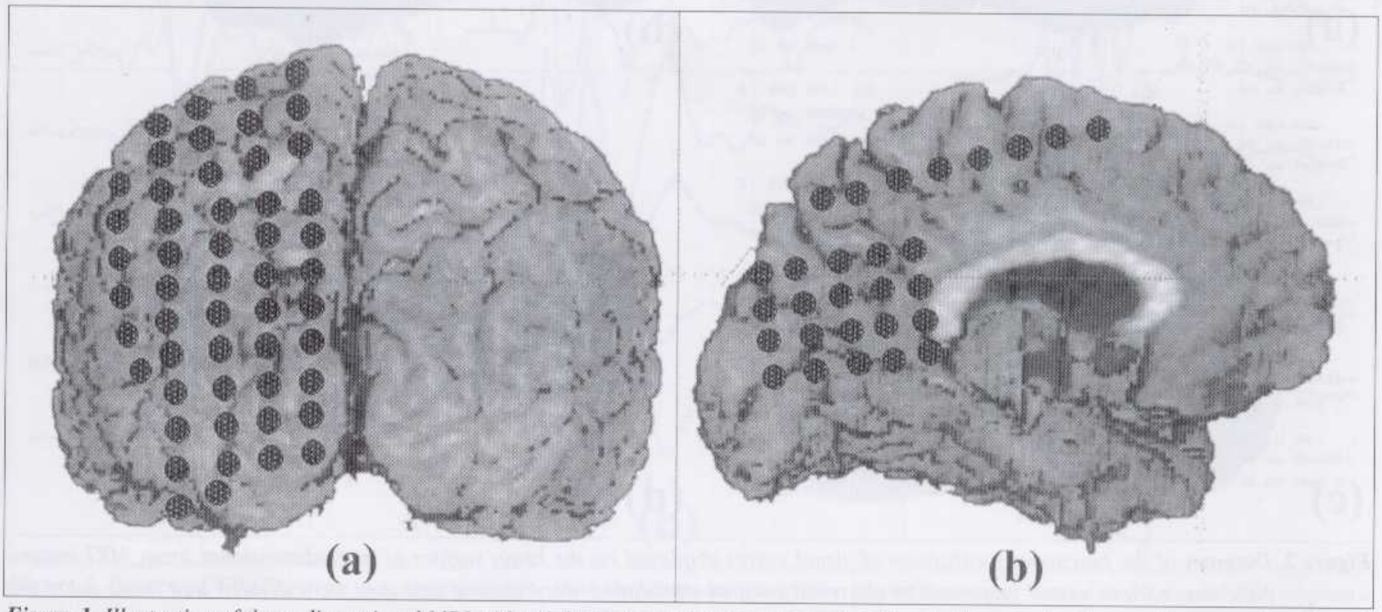

Figure 1. Illustration of three-dimensional MRI with subdural electrodes over the occipital and adjacent visual cortex in one patient. Dorsal (a) and medial (b) views. The localization of electrode position was performed using the Analyze 7.5 software (Biomedical Image Resource, Mayo Foundation, Rochester, Minn) that provides three-dimensional registrations of the brain CT and MRI scans[15].

as rainbow. For some electrodes, mainly located on the lateral superior posterior temporal or lateral temporo-parieto-occipital junction, they revealed large visual field defect on contralateral side when stimulated.

The response types of cortical stimulation were divided into three types: form, color, and moving responses. Form responses were again simple, intermediate and complex forms. For each response type, the relative distribution over the occipital and adjacent cortex were represented by percentages (Table 1) and marked over three-dimensional brain surface MRI images (Fig. 2). Simple and intermediate forms were elicited when stimulated on the electrodes over occipital pole and inferior occipital gyrus (64%) and the striate cortex (36%). Complex forms occurred when stimulated on fusiform gyrus (47%), the lateral temporal cortex (37%) and

Table 1. *The types of visual responses after electrical cortical stimulation and the anatomical distribution of each response on the visual cortex.*

Response types		
Form		
Simple & intermediate		
	Occipital pole & inferior occipital gyrus	64 %
	Striate cortex (cuneus & lingual gyrus)	36 %
Complex		
	Fusiform gyrus	47 %
	Lateral temporal cortex	37 %
	Lingual gyrus	16 %
Color		
	Fusiform gyrus	50 %
	Lingual gyrus	33 %
	Inferior occipital gyrus	17 %
Moving response		
	Medial & basal T-O or T-P-O junctions	64 %
	Lateral T-O or T-P-O junctions	31 %

T-O : temporo-occipital,
T-P-O : temporo-parieto-occipital

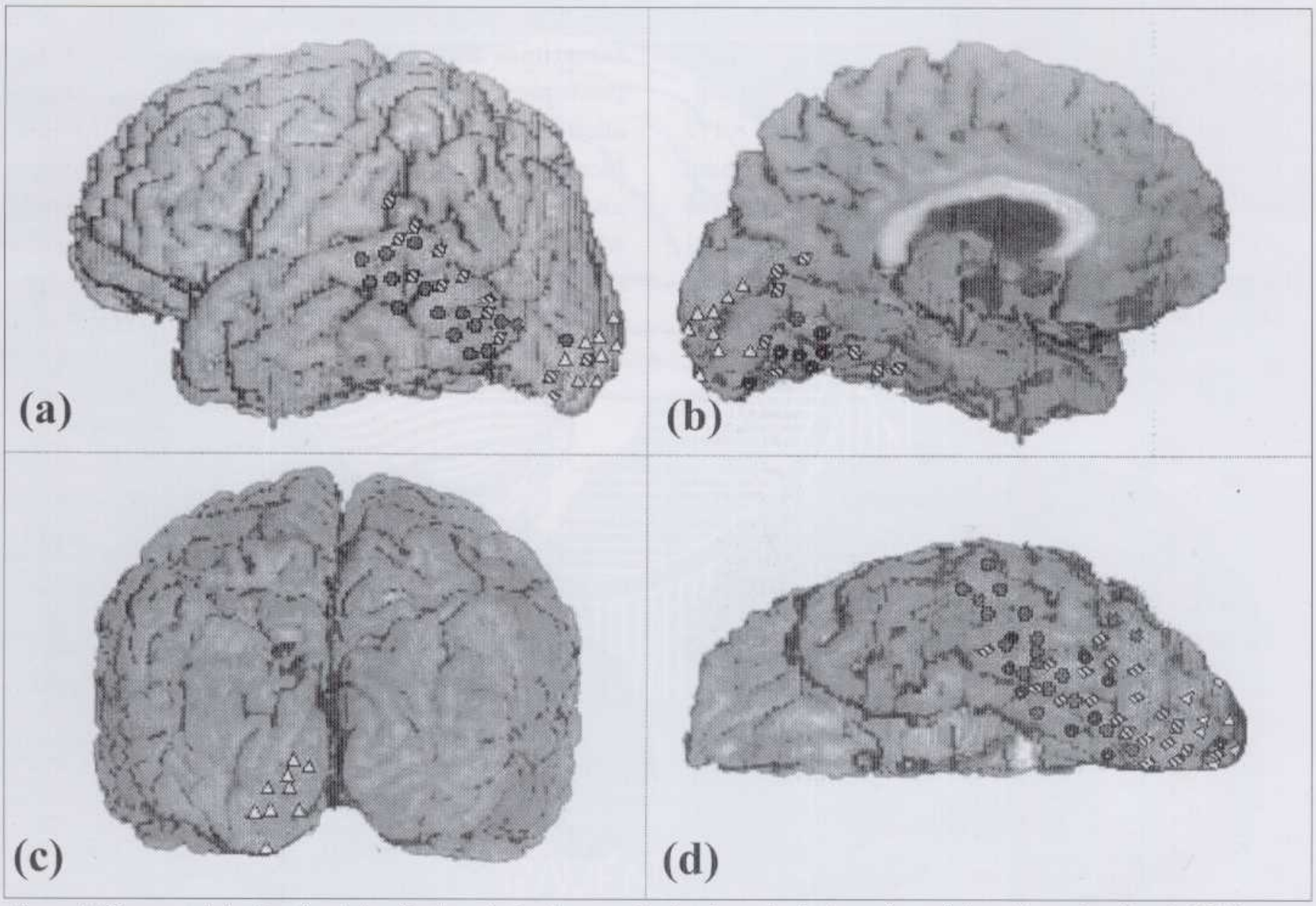

Figure 2. *Diagram of the functional localization of visual cortex displayed on the brain surface of three-dimensional brain MRI images. Note that various visual responses to electrical cortical stimulation were elicited and they were divided into form, color and motion of objects, and again form was subdivided into simple, intermediate and complex responses. Observe the distributions of such visual responses, which were demonstrated with different marks (simple and intermediate forms as △, complex form as ◍, color as ● motion as ▨ respectively). Lateral (a), medial (b), posterior (c) and basal (d) views.*

the lingual gyrus (16%). Color responses appeared after stimulation of electrodes on the fusiform (50%), the lingual (33%) and the inferior gyrus (17%). Moving responses were elicited when stimulated over the medial and basal temporo-occipital or temporo-parieto-occipital junction (64%), and the lateral temporo-occipital or temporo-parieto-occipital junction (31%).

FLASH VISUAL EVOKED POTENTIALS (FVEPs)

The types of FVEP waves were quite variable (Fig. 3). As described previously, they were classified into two main types, alternating negative to positive waves and polyphasic waves. Alternating negative to positive waves with wave I to VI were most frequently observed. The mean latency of wave IV was calculated on each anatomical location (Table 2). The cuneus showed the shortest mean latency, which was 78.4±13.9 ms. The mean latency of the occipital pole was 82.1±11.1 ms, the ligual gyrus 85.9±14.9 ms, the inferior occipital gyrus 89.6 ±7.51 ms, the lateral occipital gyrus 91.2±11.4 ms, respectively. The fusiform gyrus, the mean latency was the longest, 94.3±7.21 ms. In each patient, according to the wave IV latency, the early activation area after flash light stimulation was the striate cortex, which was anatomically including parts of cuneus, lingual gyrus just around the calcarine fissure. Farther from the calcarine fissure, even in the same gyrus, the latency was longer and longer, both to the medial and lateral sides, which reflected that functionally related areas were somewhat different from the anatomically distinct gyri. The electrodes with the shortest wave IV latency were usually located at the cuneus or lingual gyrus near the calcarine fissure, that is the stri-

***Table 2.** The latencies of wave IV of FVEPs on each gyrus of the visual cortex.*

Gyri	Latency (mean ± S.D.)
Cuneus	78.4 ± 13.9 msec
Occipital pole	82.1 ± 11.1 msec
Lingual gyrus	85.9 ± 14.9 msec
Inferior occipital gyrus	89.6 ± 7.51 msec
Lateral occipital gyrus	91.2 ± 11.4 msec
Fusiform gyrus	94.3 ± 7.21 msec

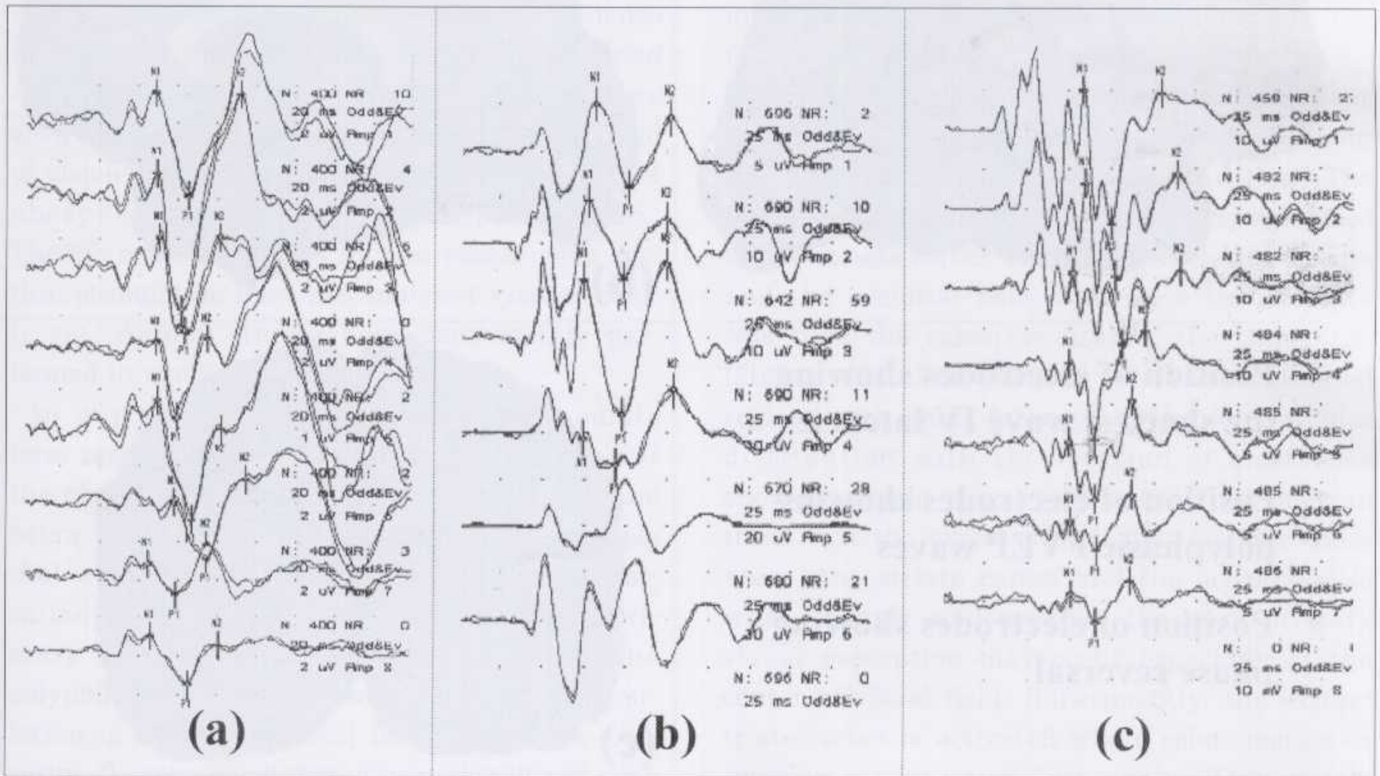

***Figure 3.** Pattern of FVEP waves in several patients. Note the alternating negative to positive waves from I to VI (a and b), polyphasic waves (c) and phase reversal (a and b). Comparing the wave IV latency, the sequential activation of the visual cortex was observed (a and b). The electrodes with short latency were located at the occipital pole and striate cortex. The polyphasic waves usually appeared at the striate and peristriate cortex.*

ate cortex, and the occipital pole (Fig. 4). The polyphasic waves were also distinguished wave type. The polyphasic waves usually appeared at the medial aspect of occipital lobe around the calcarine fissure consisting of the cuneus, the lingual or fusiform gyri, in other words, the striate and peristriate cortices (Fig. 4). The locations of the electrodes with polyphasic waves and phase reversal were marked separately (Fig. 4).

DISCUSSION

Computational tasks of vision may begin with the question from the images that *what* is present in the visual world and where it is. Visual processing involves parallel pathways from the retina to the lateral geniculate nucleus, to the striate, and finally to the extrastriate cortex. Vision has been thought to be mediated by at least three parallel pathways that process information for form, color and motion or depth. The cells in each of these visual pathways show different selectivity. In view of the research on motion selectivity, it is attractive to think that selectivity of particular classes of neurons are related to specific aspects of visual perception. Thus, orientation-selective neurons seem to provide information for the perception of shape and form, while disparity-selective neurons seem to provide information about the solidity of objects. Both types of cells could be important for perceiving *what*. Direction-selective neurons concerned with motion may tell us *where*[1].

Those results have been drawn largely from many animal studies, although its topographical arrangement of visual areas is somewhat differ-

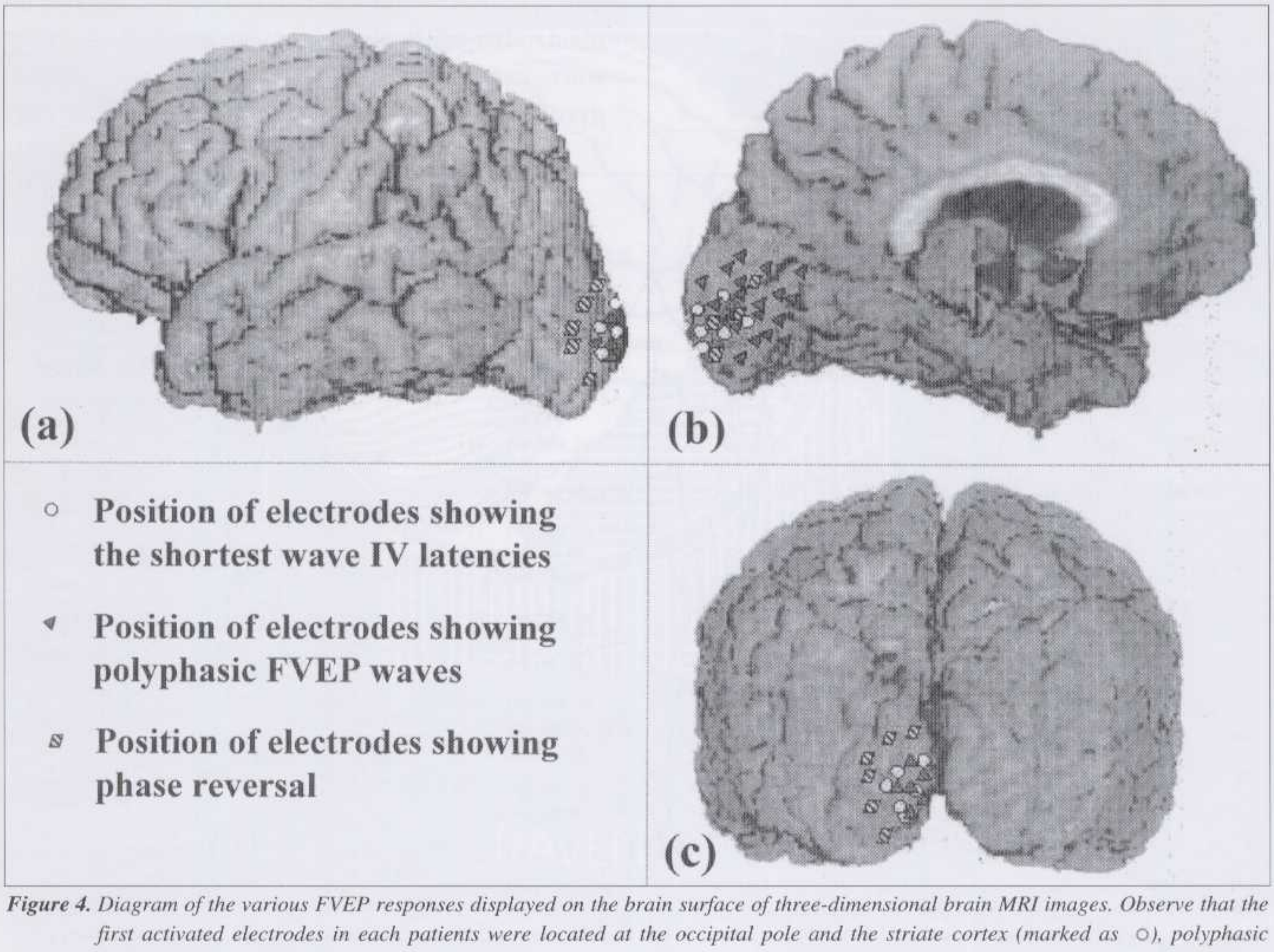

Figure 4. *Diagram of the various FVEP responses displayed on the brain surface of three-dimensional brain MRI images. Observe that the first activated electrodes in each patients were located at the occipital pole and the striate cortex (marked as ○), polyphasic waves were noted at the striate and peristriate cortex (marked as ◂), and the electrodes showing phase reversal were located along the calcarine fissure and at the lateral occipital cortex (marked as ▨).*

ent from that of human beings. The organization of the visual cortex elucidated from the anatomy and single-cell recording in the monkey, with which verbal communication is impossible. In macaque monkey, V2 surrounds V1 and is connected to it, and all modalities of vision are thought to be represented in both. V4 is well removed from V1 by other areas, in particular area V2, throughout most of its extent. Functionally monkey V4 is closely related to color response[19]. Macaque V5 is surrounded by satellite areas involved with visual motion[20,21].

Recently more information can get from the human study. As previously commented, the functional mapping of human brain cortex is essential with the progression of epilepsy surgery, so the electrical brain stimulation and evoked potentials on subdural grids are quite popular. Though the various visual responses after cortical stimulation can be observed, only fragmentary reports have been published. Till now visual field and cortical localization have been mainly reported. Most often occipital lobe stimulation produces phosphenes in the center of vision. Stimulation of the medial occipital region above the calcarine fissure induced phosphenes in the lower field contralateral to the stimulated eye, while stimulation below the calcarine fissure gave phosphenes in the contralateral upper field of vision[11,18,22,23]. Lesser et al.[11] reported quadrant phosphenes in the lateral occipital cortex. Though other aspects of human vision using cortical stimulation have not analysed systematically yet. Animal studies have been mainly performed in macaque monkey.

In our study, the simple and intermediate form responses were elicited when stimulated at the cuneus and the lingual gyrus just above and below the calcarine fissure. These findings imply that such areas just above and below the calcarine fissure are functionally related to the primary visual cortex. In some patients, the polyphasic FVEP waves were elicited on stimulation of medial occipital lobe around the calcarine fissure, suggesting the possibility of such responses associated with the primary visual processing. Complex form appeared when stimulated the basal temporo-occipital cortex, usually the fusiform gyrus, and the lateral temporal cortex, which can be thought to be an association area for higher-order visual processing. Color responses were elicited on stimulation of the electrodes over the basal occipital area, the fusiform and the lingual gyri, which is thought to be corresponding area of macaque V4. Moving responses of objects appeared when stimulating the lateral posterior temporo-occipital or temporo-parieto-occipital junctions and mesial superior temporo-occipital or temporo-parieto-occipital junctions, and those areas are thought to be human V5. The topographical separation between V5 and V4 in human visual cortex is so impressive. As far as we can tell, V4 in the human brain is located in the basal occipital area, the lingual and fusiform gyri of the prestriate cortex. Human V5 is a very unique area located in the region of the temporo-occipital or temporo-parieto-occipital junctions. In macaque monkey, additional satellite areas surrounding V5 are also activated after visual motion stimuli, which is somewhat different from that of humans[20,21]. It is possible that, with use of specific stimuli, motion-sensitive cortex surrounding macaque V5 may be demonstrated in the future.

As for a sequence of visual processing, the comparison of FVEP latency can tell us about the sequence of visual cortex activation. The electrodes with the shortest latency were located at the striate cortex around the calcarine fissure and the occipital pole. The more the distance was from the calcarine fissure, the longer the latency was. Furthermore, the early activated regions with short latency showed very similar distribution with the location of electrodes showing simple visual responses. Thus one can think that the visual stimuli first activate these areas, the striate cortex and the occipital pole where simple and precise, the very primary visual perception may occur especially at the center of visual field. Subsequently, the extrastriate cortex is activated where color, motion or complex configurations are analysed separately in functionally specialized neuronal groups. Finally, these separate attributes of vision put back together again to create a unified picture of the objects and perfect perceptual synchrony is maintained in highly organized visual cortex.

In summary, we investigated the pattern of functional organization and sequential activation in human visual cortex using electrical cortical stimulation and flash visual evoked potentials (FVEPs). These results can tell us that different areas of the human visual cortex are organized for different attributes of vision, such as form, color, and motion. And visual stimuli initially activate the striate cortex and the occipital pole, subsequently the medial and lateral occipital cortex.

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