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REVIEW

Intraoperative intrinsic optical imaging of human somatosensory cortex during neurosurgical operations

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Abstract. Intrinsic optical imaging as developed by Grinvald et al. is a powerful technique for monitoring neural function in the *in vivo* central nervous system. The advent of this dye-free imaging has also enabled us to monitor human brain function during neurosurgical operations. We briefly describe our own experience in functional mapping of the human somatosensory cortex, carried out using intraoperative optical imaging. The maps obtained demonstrate new additional evidence of a hierarchy for sensory response patterns in the human primary somatosensory cortex. [DOI: 10.1117/1.NPh.4.3.031205]

Keywords: optical imaging; intrinsic signal; intraoperative monitoring; human somatosensory cortex; neurosurgical operation.

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1 Introduction

Optical imaging of neural activity in the *in vivo* central nervous system (CNS) is based on the extrinsic optical signals obtained with voltage-sensitive dyes (VSDs) and the intrinsic optical signal without VSDs.[1–3] In the imaging of membrane potential changes in the CNS, it is known that voltage-dependent extrinsic optical signals are often distorted and/or contaminated by slower intrinsic optical signals.[4,5] In response to these preliminary observations, Grinvald et al.[6] have developed a unique intrinsic optical imaging technique for monitoring cortical activity.

The intrinsic optical signal detected *in vivo* in the CNS is considered to be at least three different components: (1) activity dependent changes in the oxygen saturation level of hemoglobin; (2) changes in blood volume in an area containing electrically active neurons; and (3) light-scattering changes that accompany cortical activation, which are caused by ion/water movement, expansion and contraction of extracellular spaces, capillary expansion, or neurotransmitter release.[5–8] Components 1 and 2 dominate intrinsic signals at wavelengths of incident light between 400 and 630 nm, while component 3 becomes a significant source of intrinsic signals above 630 nm and dominates the signals in the near-infrared region above 800 nm.[7] As pioneered by Grinvald et al.,[9] this method has been applied widely to various regions in the mammalian CNS, e.g., the cat/monkey visual system (for reviews see Refs. 10 and 11), the rodent somatosensory cortex (for a review see Ref. 12), the rat spinal cord,[13,14] and the rat brainstem.[15]

2 Intraoperative Intrinsic Optical Imaging of Human Brain Function

Intrinsic optical imaging is applicable to the human cortex during neurosurgical operations because of its dye-free nature (for reviews see Refs. 16 and 17). Functional imaging of the human brain has significant uses in basic medical and clinical physiology. During surgical operations on brain tumors and intractable epilepsies, operators need to obtain functional local maps of the human brain for making decisions regarding the resection area.

Intraoperative intrinsic optical imaging of human brain function was first reported by Haglund et al.[18] They succeeded in monitoring stimulation-evoked epileptiform after discharges and cognitively evoked functional activity in the human cerebral cortex. Subsequently, intraoperative intrinsic optical imaging has been carried out by some groups to monitor brain function related to sensation,[19–29] language task,[30,31] tongue movement,[32] and intractable epilepsy.[33,34]

In general, the imaging apparatus is composed of image forming optics, a detector, and an acquisition computer. In our laboratory, a charge coupled device camera fitted to an operating microscope detected reflected light from the cerebral cortex, which passed through an interference filter with a passband at 605 ± 5 nm. This wavelength produced the largest optical signals in rat whisker barrel experiments.[35,36] Signal acquisition and imaging were performed using differential video acquisition systems, IMAGER 2001 (for Fig. 1) or IMAGER 2001 VSD+ (for Fig. 2) (Optical Imaging Ltd., Germantown, New York). These recording systems were developed in Professor Grinvald's laboratory and the newest version is available from Optical Imaging Ltd.

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Under informed consent, we have measured intrinsic optical signals from the cerebral cortex in 30 anesthetized patients undergoing surgery for brain tumors (27 patients) and intractable epilepsies (3 patients). In the 30 patients, we succeeded in mapping brain function in 26 cases. In Secs. 3 and 4, we introduce two functional mappings of great interest obtained in the human somatosensory cortex.

3 Functional Mapping from Subdivisions of the Primary Somatosensory Cortex

In an electrical stimulation study on the human cerebral cortex during neurosurgical operations, Penfield and Boldray[37] demonstrated that the human somatosensory cortex is a highly sophisticated system for information processing. The primary somatosensory cortex is subdivided into four cytoarchitectonic areas, which are termed Brodmann's areas 3a, 3b, 1, and 2.[38,39] Physiological and anatomical studies of nonhuman primates have shown that there is a complete topographic representation of the body in each of the four Brodmann's areas, and that these areas exhibit a hierarchy in sensory information processing (for a review see Ref. 40). Using intraoperative intrinsic optical imaging, we directly showed a similar hierarchy in the human primary somatosensory cortex.

Figure 1 shows an example of intrinsic optical images induced by individual stimulation of digits I and V in a 57-year-old patient. In this case, we identified two separate response areas for each digit stimulation, areas I_1 and I_2 and areas V_1 and V_2 [Fig. 1(a)]. Areas I_1 and V_1 were located near the central sulcus, whereas areas I_2 and V_2 were located near the postcentral sulcus. Interestingly, response areas near the central sulcus were completely separate from each other, whereas those near the postcentral sulcus were partially overlapping. A difference in the time course of the optical signal was seen between the two areas, although the time resolution of the present study was not so high (about 0.7 s) [Fig. 1(b)]. Similar maps were also obtained in four other cases (three in the finger region and one in the face region: see Figs. 6 and 7 of Ref. 24).

Where are the origins of these optical response areas? The borders of Brodmann areas 3a, 3b, 1, and 2 are somewhat different between studies. If we consider that the response areas near the central and postcentral sulci correspond to Brodmann area 1 and 2, respectively,[38,39,41] our maps might indicate that neurons in Brodmann area 2 receive sensory information from larger peripheral fields than those in Brodmann area 1. Similar observations have been reported in the monkey somatosensory cortex.[42–45] On the other hand, if we consider that Brodmann area 1 occupies the crown of the postcentral gyrus and reaches

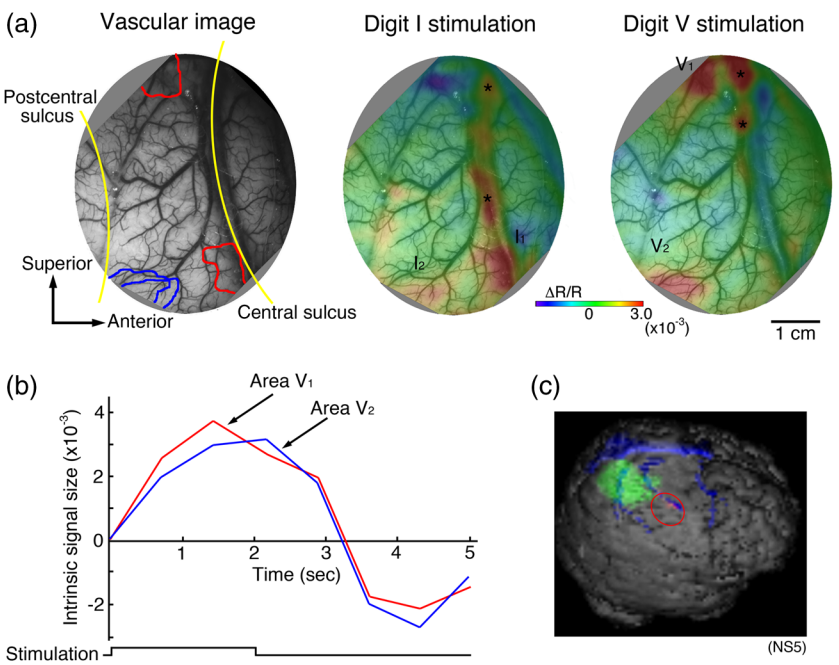

Fig. 1 (a) A vascular image of the recording region and color-coded images of intrinsic optical signals induced by digits I and V stimulation. The digits were individually stimulated transcutaneously with surface electrodes driven by an electrical stimulator at 5 Hz for 2 s. The detected optical signals are superimposed on the vascular image. Eight images were collected in 5 s (1 frame/0.7 s) from the right somatosensory cortex of a 57-year-old patient who suffered from anaplastic oligodendroglioma, and the first one was used as a reference image. Both digits I and V stimulation induced two separate response areas, areas I_1 and I_2, and areas V_1 and V_2, respectively. Asterisks indicate noise due to blood flow. In the vascular image, the yellow curves indicate the central and postcentral sulci, and the red and blue curves show the digits I and V response areas identified in the color-coded images. The optical response area for each finger stimulation was defined as the area with the fractional change $(\Delta R/R) > 2.0 \times 10^{-3}$. (b) Time courses of changes in the intrinsic optical signal size in area V_1 (red line) and area V_2 (blue line). The positive direction corresponds to a decrease in light reflectance. (c) The recording site of the intrinsic optical signals is illustrated with a red ellipse on a three-dimensional (3-D) magnetic resonance (MR) image. The green area indicates the brain tumor. The major veins are illustrated in blue. See Ref. 24 for more details.

down into the postcentral sulcus,[46,47] it is possible that further functional subdivisions exist in Brodmann area 1.

4 Overlapping Representations in the Primary Somatosensory Cortex

In the primate, Kaas et al.[48] showed complete somatotopic maps in each Brodmann area (3a, 3b, 1, and 2) with microelectrode recording. In the monkey somatosensory cortex, significant overlapping representations of fingers were found in the somatotopic maps. Do similar overlaps exist in the human brain?

Figure 2(a) shows an example of intrinsic optical images induced by individual stimulation of digits I–V in a 47-year-old patient. The recording site corresponded to the postcentral gyrus, and optical responses induced by digits I–V stimulation were clearly identified in different regions of the primary somatosensory cortex. Figure 2(b) shows functional maps of finger representations in the somatosensory cortex obtained from four different patients. In these maps, we could not clearly identify subdivisions in the primary somatosensory cortex shown in Fig. 1, possibly because of differences in measurement conditions. Nonetheless, these maps show that (1) optical response areas induced by digits I–V stimulation were sequentially aligned along the central sulcus in the crown of the postcentral gyrus; (2) the digit I area was located in the most latero-inferior

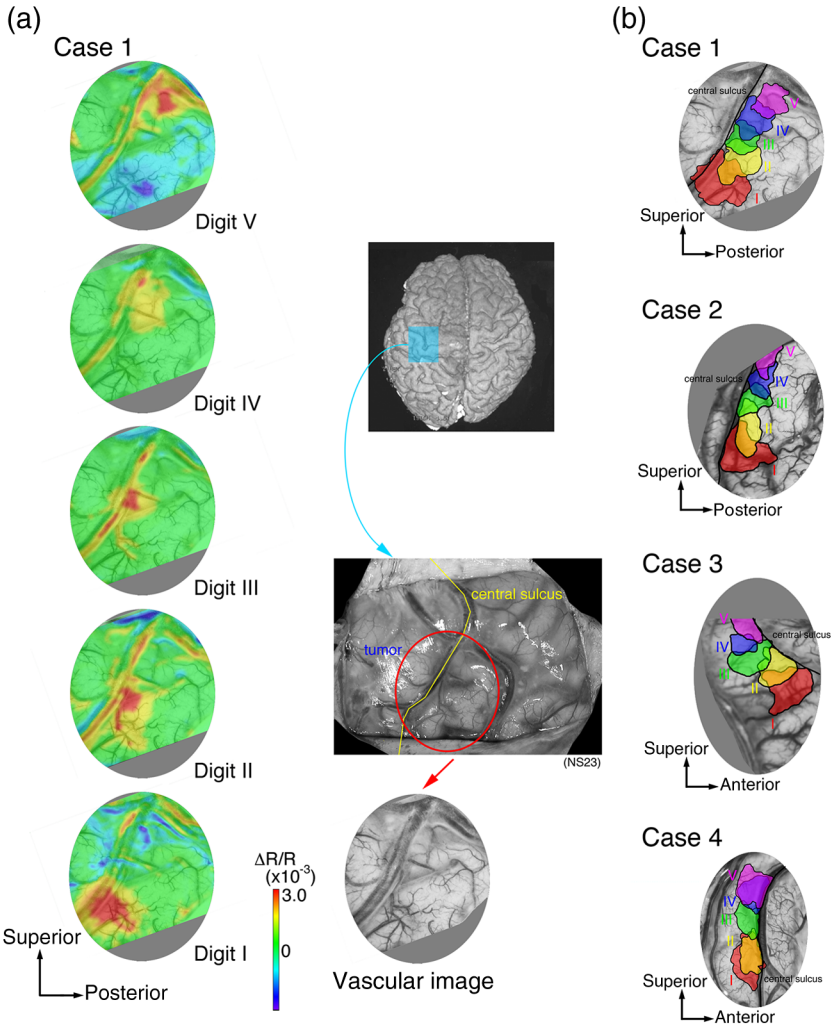

Fig. 2 (a) Color-coded images of intrinsic optical signals induced by digits I–V stimulation. Right digits I–V were individually stimulated with surface electrodes driven by an electrical stimulator at 5 Hz for 2 s, and intrinsic optical signals were recorded from the left somatosensory cortex of a 47-year-old patient who suffered from an oligodendroglioma. The detected optical signals are superimposed on the vascular image (left panels). The recording site is shown on a 3-D reconstructed MR image with a blue rectangle and on a photograph of the cortical surface with a red ellipse. The yellow line indicates the central sulcus. The central sulcus was determined by recording somatosensory evoked potentials in response to median nerve stimulation. The vascular image obtained at a wavelength of 540 nm is also shown in the lower right panel. (b) Functional maps of finger representations in the somatosensory cortex obtained from four different patients (cases 1 to 4). The optical response area for each finger stimulation was defined as the area with the fractional change $(\Delta R/R) > 1.5 \times 10^{-3}$. The response areas of different fingers are shown with different translucent colors (digit I: red; digit II: yellow; digit III: green; digit IV: blue; and digit V: red purple), and are superimposed on the vascular image. Each response area is outlined with a black solid curve. Maps were obtained from the left (cases 1 and 2) and right (cases 3 and 4) cortices. See Ref. 26 for more details.

region, whereas the digit V area was located in the most mediosuperior region; (3) in most patients, the digit I area was the largest and the digits III–V areas were smaller; and (4) the neighboring response areas partially overlapped each other, and had interindividual variations. Similar overlapping representations were also observed in the face region of two patients (Fig. 5 of Ref. 26).

Considering these maps together with previously reported observations in nonhuman primates[23,45,49,50] and humans,[21,25] the overlap of the activated areas is considered to be a common characteristic in the somatosensory cortex not only in nonhuman animals, but also in humans. This overlap might be functionally important in sensory information processing.

5 Conclusion and Further Considerations

Intrinsic optical imaging has the best combination of spatial and temporal resolutions for mapping human brain function. Advances in intrinsic optical imaging of neural function have benefited from the development of imaging techniques by Grinvald et al. The high success rate for functional brain mapping implies that the intraoperative intrinsic optical imaging is a powerful and reliable method for evaluating human brain function during neurosurgical operations. Evaluation with functional brain mapping enables neurosurgeons to perform much more accurate operations. On the other hand, there are some points to be improved and considered to obtain clearer functional maps during the limited recording time. First, the human brain exhibits large mechanical movements due to respiration and cardiac beats, which require the stabilization of the cortex by a glass plate and a lot of signal averaging. To reduce the recording time, it should be necessary to develop new methods for stabilization of the cortex in addition to the hardware improvement. Second, the arachnoid membrane is often thickened in brain tumor patients, especially in elderly persons. In such cases, it is difficult to rule out movement artifacts from true signals as shown in Fig. 3 of Ref. 26. It seems very important to carefully consider the condition of the brain before optical imaging.

Disclosures

The authors have no competing interests to disclose.

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