A WAY TO LEARN BRAIN FUNCTION

Functional Magnetic Resonance Imaging (fMRI) of the brain is a way to learn brain function. It has been extensively used in brain science. It points out which parts of the brain are used when the brain performs a given functional task. It can identify the functional roles of such brain units. However, fMRI does not detect directly the electrical neuronal activity induced by the task, but it depends on the secondary physiological responses, such as changes in metabolic activity and cerebral blood circulation, associated with the neuronal activation. There are two very fortunate situations nature provided for us. One is the fact that the brain is subdivided in distinct many functional units rather than it works as a whole. If there is no spatial distinction, there is no point to make image. The second is that the responses in metabolic activity and blood circulation are very tightly coupled to and roughly co-localized with the neural system activity of these functional units. Recently this feature of the tight coupling has been experimentally shown. If any of the two fortunate situations is absent, so-called functional neuro-imaging does not exist.

MRI is known as the best non-invasive method to measure anatomical structure of the brain. It can depict the detailed structure with contrast based on the subtle variation of magnetic characters of water protons. Such magnetic characteristics depend on the local environment in which these water molecules are placed. Although to measure anatomic structure is the most important objective for MRI usage, the image is rather static. In late 1980's, we were seeking some dynamic aspect in MR images, some signal changes that could depend on the physiology or hopefully on the function of the brain. One of such phenomena we encountered was the image contrast that depended on the concentration of hemoglobin with ferrous iron without bound oxygen.

We called the image contrast BOLD (Blood Oxygenation Level Dependent) contrast. It is due to the presence of hemoglobin in the blood. Hemoglobin after unloading oxygen to the tissue is paramagnetic (deoxyhemoglobin). On the other hand, hemoglobin combined with oxygen (oxyhemoglobin) is diamagnetic. This magnetic property of hemoglobin that is determined by the state of the ferrous ion at the middle of the heme has been known since Linus Pauling showed it in 1930's. When deoxyhemoglobin molecules in red cells are placed in a magnetic field, they induce some small magnetic field perturbation in and around the blood vessels, as small weak magnets could do. Water protons in such environments sense these field disturbances. As a consequence, MRI signals in these locations show small intensity drop and make image contrast relative to the location with no signal drop. On the other hand, diamagnetic oxyhemoglobin whose magnetic property is not much different from the surrounding tissue does not produce the field disturbances. The amount of deoxyhemoglobin varies with the physiology, namely the blood flow (oxygen supply) and metabolic activity (oxygen consumption). Furthermore, when a part of the brain is activated to perform a functional task, the physiology at the location changes accordingly as mentioned earlier. Therefore, MRI signal can have some sensitivity toward the functional activity in the brain. At the beginning of the last decade, we postulated the potential of MRI for such functional imaging as PET (positron emission tomography) that was already known at that time.

The success in capturing functional responses in the human brain was brought out by the collaboration with Prof. Kamil Ugurbil at University of Minnesota and his young able

associates, such as Drs R. Menon, S.G. Kim and others. We all shared the excitement at the time of the success. By the time the result was published in 1992, two other groups, Milwaukee College of Medicine and Massachusetts General Hospital of Harvard University, reported their results within a few weeks apart. Immediately afterwards, a large number of enthusiastic scientists worked hard to develop the field now known as fMRI and the scope of the research field has expanded widely into the brain science.

Meanwhile, alternate methods for fMRI in addition to BOLD have been developed. They include those to measure changes in CBF (cerebral blood flow) and CBV (cerebral blood volume). BOLD imaging which depends on deoxyhemoglobin reflects the change in the downstream side of the circulation from capillaries to veins. CBF measurements focus on the change in arterial side of the blood circulation. Among these methods, BOLD imaging, because of its sensitivity and convenience of measurements, is still most popular for application in cognitive neuroscience and clinically oriented research.

The features of fMRI are that the measurement is completely non-invasive, comes with reliable structural information at relatively high spatial resolution and is real time measurement at a rate of covering whole brain area in a few seconds or one slice image within less than 100 milliseconds. These features make fMRI be a choice among the methods now known for functional study of the brain. On the other hand, fMRI also has shortcomings, mostly due to the fact that it is based on the secondary response to the neural activation. These include a slow response time of seconds rather than tens of milliseconds in which neural processes proceed. Another is the presence of physiological signal variation at similar size to the fMRI signal. The local signal change of fMRI is sitting on the occasional variation of live brain circulation. It requires further technical advances to distinguish the two better.

Non-invasiveness of fMRI measurement allows normal willing volunteers to participate in the examination as well as those people with some neuro-disorder. The potential for the clinical application can be seen in the feature. These merits as above have made the method be a major tool for neurophysiologists or cognitive neuroscientists to study the functional map of the brain. Such mapping can cover the primary and secondary areas for sensory inputs, motor areas for execution and processing areas for preparation and control of motor motion, areas in the brain attributable to psychophysical phenomena. Mapping study further includes areas for higher order cognitive function such as language, short- and long-term memory and even emotion. FMRI does not detect the activity of individual neurons, but measures the system activity of functional units and therefore it fits for the mapping.

FMRI is a way to learn brain function as said earlier. It is 'a' way and also only one aspect of the brain function can be touched with it. That is to show the location where the action for a specific task is. In the coming years it will refine the knowledge of the specificity of the functional site further, but never tells the content of the processing or what is being done at the activated area. What kind of language the brain is using to communicate and to process within the brain itself is yet to be found in brain science in general. Functional neuro-imaging will contribute to lay down some parts of the framework on which neuroscientists will build the way to the final understanding of how brain works.