特集 最新検査法の小児頭部画像診断への応用

3. Pediatric fMRI/EPI

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Abstract

Rapid advances have occurred in pediatric neuroimaging over the past five years, especially in the area of so-called "Functional imagining" and in particular functional magnetic resonance imaging (fMRI). This has been accele rated by the introduction of echo-planar imaging (EPI), which allows for the very fast acquisition (<100 ms/image) of multi-slice images. Pediatric radiology is no longer just a question of interpreting anatomy, for with the ability to combine structure with function, we are now able to extract physiological information. This opens up exciting possibilities for advances in the field of neuroscience, particularly in the pediatric arena. This review will discuss the background, current status of and future possibilities for pediatric fMRI.

Keywords : Functional MRI, EPI, Pediatric Neuroimaging

Definition

Functional MRI can be defined as the utilization of an MRI sequence to determine a parameter not normally seen by conventional MR imaging. The combination of that parameter with the high spatial resolution of conventional MRI leads to the demonstration of functional anatomy or physiology. FMRI of the brain can thus be considered to include activation fMRI, perfusion, diffusion-weighted imaging and MR spectroscopy. For the purpose of this paper the discussion will be restricted to the consideration of activation fMRI.

Background

Functional MRI is based on the original observations of Roy and Sherrington[1], at the turn of the century, who showed - amongst other things* that changes in blood flow and metabolic activity paralleled each other. Other important advances in terms of neurophysiology were made by Penfield and co-workers[2,3], who mapped the sensory and motor cerebral cortex in higher primates and man by observing the effects of direct electrical stimulation.

In 1988, an early report of dynamic imaging in normal brain appeared[4], which used the magnetic susceptibility effects of exogenous contrast material to trace cerebral blood flow. This was soon followed by an article on functional cerebral imaging using susceptibility-contrast MRI[5]. In 1990, Ogawa et al[6], reported oxygenation-sensitive MRI signal changes in rodent brain at high magnetic fields, which did not require the administration of any extrinsic contrast agent but relied on the alteration in oxy -/deoxy* hemoglobin ratio in normally circulating blood following delivery of oxygen to tissue. This technique, known by the acronym BOLD, was applied using a 1.5T echo-planar (EPI) fast acquisition MRI system to map the activated human visual[7], sensory[8,9] and motor cortices[10], as well as Broca's motor area for language[11]. The fMRI paradigm was subsequently translated to non echo-planar systems[12,13].

FMRI sequences

Blood oxygen level dependent (BOLD) contrast imaging is based on the observation that the brain shows localized blood volume increases upon neuronal activation. It has also been shown that these increases far exceed the oxygen consumption of the tissue. Therefore, the venous oxygen content increases and yields an increase in the MRI signal observed. This is due to the fact that deoxyhemoglobin is paramagnetic which directly affects the local susceptibility of the tissue. It generates an inhomogeneous magnetic field in tissue surrounding blood vessels, causing intravoxel dephasing and decreased signal intensity on MR images. These local variations in susceptibility in the region of the blood vesels contribute to the apparent transverse rela xation time T2*. As the venous and capillary oxygen content increases, the amount of deoxyhemoglobin in the blood decreases, which increases the MR signal. Thus, changes in the local functional activation can be detected by any pulse sequence which is sensitive to T2*. In conventional scanners, this sequence is a gradient echo train.

While it has long been recognized that brain cortex has a much richer vascular supply than the underlying white matter, there has been much controversy as to the relative contributions of capillaries versus venules to the BOLD signal. Observations on the EPI time course of fMRI at 4T have demonstrated a multiphasic response in the occipital cortex to photic stimulation[14], suggesting a sensitivity to capillaries in the gray matter at high field strengths. This probably still leaves a significant signal contribution from larger vessels, such as draining veins, at the more standard 1.5T field strength.

EPISTAR is another technique for fMR imaging using echoplanar imaging and signal targeting with alternating radiofrequency[20]. This method relies upon a process known as pre-saturation to generate a perfusion map. Also described as spin tagging, the principle of pre-saturation utilizes the relatively long T1 relaxation times of protons to initially reduce the MR signal in all protons located inferior to the imaging slice being studied. he spins within the imaging slice are already saturated by the excitation pulses from the preceding pulse sequence. By directing a saturation RF pulse to the spins in the tissue volume immediately inferior to the imaging slice, EPISTAR induces a blood flow dependent decrease in MR signal within the imaging slice. This signal change occurs as the low-signal pre-saturated spins in the blood flow upward into the imaging slice. If no pre-saturating pulse is administered, the signal within the imaging slice will change in the opposite direction, increasing in intensity. Here, the spins in blood from outside the slice are fully relaxed and move into the imaging slice to brighten the image. Comparison of the images with each of the alternated radiofrequency images generates a perfusion map that indicates cerebral blood flow.

Task-based fMRI has been performed with both EPISTAR and BOLD techniques in a comparison study[21]. Volunteer subjects were asked to perform a sequential finger-thumb opposition task and EPISTAR or BOLD fMRI was done to capture regional cortical activation. Activation in the perirolandic region was seen using both techniques, with no significant differences between them.

Data acquisition

With the standard gradient echo images at 1.5T, the change in signal when the brain is activated is typically on the order of 2～10%. Since noiseint he image is typically on the order of 1～2%, this results in many problems in deciding what is activation and what is noise. Therefore, the most commonly used method of data acquisition is the so-called 'ox-car* design, where periods of rest are alternated with periods of activation by a paradigm designed to specifically stimulate one area or function of the brain during the performance of the fMRI. The images are then subtracted and compared statistically on a pixel-by-pixel basis to reveal any areas of functional activation. With the more widespread availability of echoplanar hardware and software up grades, not only has the acquisition time for fMRI come down to tens of milliseconds but image resolution has also improved along with improvements in signal to noise ratio.

Another factor that has to be taken into consideration when acquiring fMRI data is the question of misregistration from patient motion during the study. Motion correction algorithms and re-registration techniques are widely employed in an attempt to compensate for this[15,16]. This is of special consideration when dealing with children where the speed and simplicity of study design, absence of artefact producing metal such as braces or other orthodontic hardware and a knowledge of the level of patient co-operation are all important factors in the successful completion of pediatric fMRI in the awake child.

Behavioral training in preparation for fMRI

Our institution is equipped with (a) a 'mock* scanner that closely resembles an actual scanner, down to a tape of the sequence noise, (b) a custom-designed, computerized head movement detection program and, (c) an audiovisual entertainment system that includes a television at the foot of the table and earphones for the child to wear. Together these three components function in a feedback loop to provide immediate visual and auditory information to the child about his/her movement during a practice trial. Head movement is measured by a fiberoptic sensor affixed to the child' s head and, ultimately, made evident to the child as a temporary interruption in the video they have chosen to watch through a system of mirrors on the headcoil[17,18].

Typical training proceeds as follows. After interviewing the child and his/her guardian(s) and introducing them to the facility, a treatment plan and reinforcement system of rewards for success is developed. Baseline data on head movement and tolerance for being in the bore of the magnet is collected and reviewed. The child is then carefully challenged with systematic manipulation of the threshold for acceptable movement and scanning time so that he/she learns to feel comfortable with the procedure and equipment. This process is carried out by the nursing staff with the assistance of a neuropsychologist. Once the child has learnt to lie still for an acceptable scanning time interval, the actual fMRI is undertaken.

Study design

One of the single most important aspects of fMRI is the development of an appropriate paradigm to accurately test the function that the investigators are concerned with. Increasingly this has become a multidisciplinary task requiring input not only from the radiologist who can help in the design with their knowledge of the interplay between the patient, equipment and sequences involved, but also the pediatric neurologist and neuropsychologists as well as the physicists who will implement it and be involved in the statistical analysis and post-processing of data. As can be seen no one person holds all the knowledge and information required to successfully develop new paradigms, especially as new questions are developed the answers to which are as yet unknown. Faulty task design will only lead to confusing results which will be uninterpretable or at worst misinterpreted.

Post-processing

Many methods of post-processing the large amount of data generated by an activation fMRI sequence have been developed and it is not unusual for the analysis of a multislice echoplanar data set to take a minimum of 2 hours to complete and sometimes much longer. Taking the simplest case of a single slab gradient echo BOLD sequence the fundamental principal, after any motion correction has been carried out, is to perform some test of statistical signific ance on the raw data to produce a 壮tatistical parametric map* (SPM). A thresholding correlation is then set, say to a value of $P<0.01$ to further remove data points which are likely to represent noise and help clean up the image.Integration of the thresholded SPM with the anatomic image is then performed in order to produce the final image, see Figs. 1B &1C. There are now several

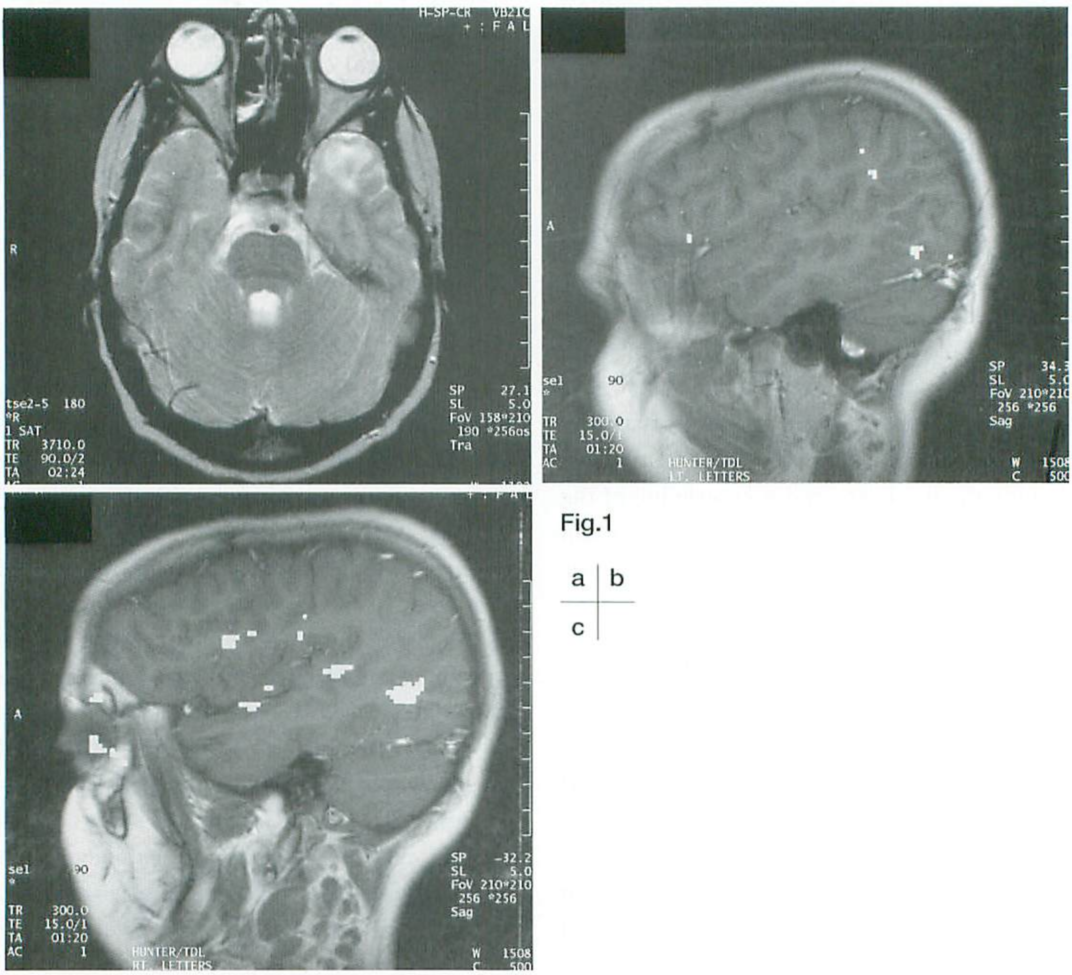

Fig.1

a | b
c

a : Axial T2-w image in a 13-year-old right-handed boy with intractable TLE, demonstrating increased signal returned from the left anterior temporal pole, proven at subsequent resection to be a left temporal lobe dysgenesis.

b : Sagittal 5㎜ single slab BOLD technique using FLASH sequence (Siemens, Somatom 1.5T) through the pathology in the left temporal and in the expected plane of Broca' s and Wernicke' s areas, demonstrating signal returned from the occipital cortex.

c : Sagittal 5㎜ single slab BOLD technique through the right fronto-temporal region demonstrating signal returned from the expected positions of Broca' s (frontal cortex) and Wernicke' s (superior temporal gyrus) areas for expressive(motor) and receptive language respectively. This was concordant with the subsequent Wada test. Note that increased blood flow is again appreciated in the visual cortex.

'off the shelf* and commercially available packages for handling echoplanar datasets, such as SPM and AIR including routines for 'warping * brains to a Talairich atlas[19] in order to pool data and compare across and between patients. This methodology may work for the anatomically normal adult brain but should be used with some reservation in the growing brain and especially where there is distortion of normal architecture by, for example, tumor.

Clinical applications of pediatric fMRI

The most often requested use of fMRI in the pediatric population is from the neurosurgeon, to noninvasively map functional brain tissue and localize areas of eloquence with respect to pathological areas of brain. This has trem endous utility in pre-surgical planning to minimize the risk of damaging the child and to pre-plan the surgical approach. We have had good experience of this at our institution (Ⅰ)utilizing finger-thumb opposition to outline sensorimotor cortex and define displacement of the central sulcus in relation to a space-occupying lesion, (Ⅱ) using LED goggles to stimulate visual cortex prior to re-operation in a patient with a partial field cut (**Fig. 2**) and (Ⅲ) using a covert letter and word generation paradigm to identify hemispheric dominance for language before temporal lobectomy in children with intractable complex partial seizures[22], (**Fig. 1**). Research from other authors wo uld appear to corroborate our findings[23-25].

Future directions of pediatric fMRI

We have shown the feasibility of performing fMRI in children including the performance of visual fMRI in the sedated infant[28]. Future applications of fMRI include the potential to replace Wada testing in children by a combination of language task for determining hemispheric dominance for language in addition to a memory paradigm in patients with temporal lobe epilepsy[30]. Some authors have reported the use of fMRI to detect rapid brain metabolic changes in infants[26]. Work is currently in progress on the changes in functional activation patterns during normal development[27], and we have addressed the issue of visual cortex activation in children with congenital structural abnormalities[28]. Other areas of potential future research include the elucidation of the neurobiological basis for neuropsychiatric disord ers such as obsessive-compulsive disorder[29], and attention deficit disorder (ADD). The whole question of plasticity following an early insult to the infant brain may lend itself to investigation by a noninvasive test such as fMRI and there a myriad of questions concerning gender differences that remain to be answered.

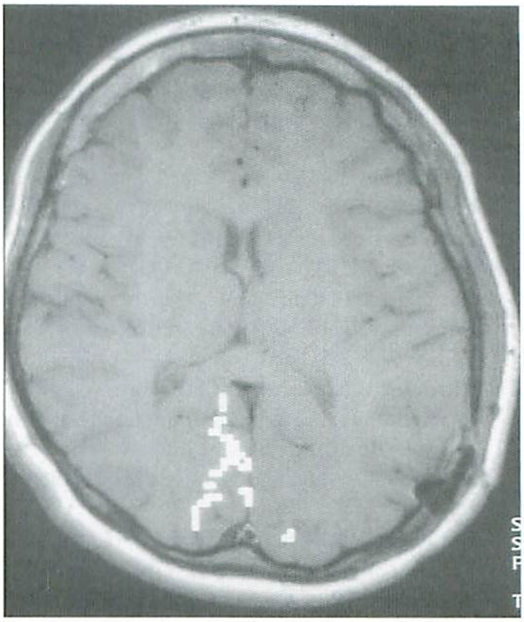

Fig.2

Axial slice from an echoplanar BOLD fMRI, with functional map superimposed on conventional MR image, in a girl with appropriate field cut following recurrence of a left occipital astrocytoma (note the susceptibility artefact from the prior left occipital craniotomy). Visual stimulation to both eyes revealed decreased signal in the left calcarine cortex and was used to map visual cortex in planning the subsequent surgery which was successfully performed without additional visual loss.

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和文抄録

ここ5年で小児の神経画像診断には急速な進歩がみられた．その中でもいわゆる脳機能画像（Fuctional Imaging），特にfunctional MRI（fMRI）といわれる手法においてそれは著明である．fMRIは100ms以下の超高速で複数スライスの撮像を可能にしたエコープランナー法（EPI）の導入により加速された．小児放射線診断はもはや解剖を解釈するだけのものではなくなり，機能と構造を連合することができる．つまり，われわれは生理学的情報をひきだすことが可能となったのである．この事実は神経科学の分野，特に小児領域での非常に楽しみな進歩の可能性を開いた．本稿では，小児のfMRIの背景，現状と将来的な可能性について述べる．

（和訳　相田典子）