Functional magnetic resonance imaging in adult craniopagus for presurgical evaluation

Case report

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Cranially conjoined twins are rare and pose unique challenges in the preoperative evaluation of cerebral language function. The authors report on their experience in the functional magnetic resonance (fMR) imaging evaluation of adult craniopagus (temporoparietooccipital fusion) to evaluate hemispheric language dominance and the eloquent language areas in the preoperative planning stages. Conventional clinical imaging hardware originally designed for individuals was adapted and tailored for use in the twins. They were assigned a selection of language tasks while undergoing fMR imaging. Significant blood oxygen level–dependent activations were detected in the main language regions in each twin, that is, the inferior frontal gyrus (around the Broca area), the middle and superior temporal lobes (around the Wernicke area) together with the inferior parietal lobe, and the middle and superior frontal gyri. Overall, the right-handed twin was strongly left lateralized for language, whereas the left-handed twin showed more bilateral activation during language tasks. Noninvasive language mapping with the aid of fMR imaging has been demonstrated for the first time in total craniopagus.

Key Words • craniopagus • conjoined twins • functional magnetic resonance imaging • blood oxygen level–dependent technique • language mapping • language dominance

Conjoined twins are uncommon, with an estimated incidence of between one in 50,000 and one in 80,000 births. Of these, cranially conjoined twins, or craniopagus, are even rarer, with an incidence of one in approximately 2.5 million births.20,31,48 The evaluation of craniopagus, particularly when the twins are adults, poses unique challenges to the attending radiologists and neurosurgeons. Accurate imaging of the anatomical fusion, the morphological characteristics of the underlying structures, and the vascular anatomy is important in guiding decision making, surgical planning, and prognostication of outcome.

Apart from the structural/morphological evaluation, a proper assessment of the functional areas is important in understanding and defining the underlying pathophysiological status of the brain before surgery is performed. Determination of which brain areas control language function as well as the cerebral hemispheric language dominance is desirable, particularly in cases in which the site of fusion involves the temporal and parietal lobes. Defining eloquent language areas will help guide the surgical approach if surgery is performed, thereby minimizing morbidity. Although assessments of other cases of craniopagus soon after birth have typically focused on structural/morphological aspects, the maturity of the patients in the present case made possible and necessitated the assessment of language functionality. Our findings should provide interesting data on language laterality in twins, which has been postulated as genetically influenced and correlated with handedness.18,23,41,45 Such information might be obtained noninvasively by using fMR imaging studies with the BOLD technique. We report on our experience in the fMR imaging evaluation of adult craniopagus to map eloquent language areas during presurgical evaluation. To our knowledge, this is the first reported case of fMR imaging in craniopagus in the medical literature.

Case Report

History. One pair of 27-year-old female conjoined (total parietotemporooccipital craniopagus) twins were evaluated to determine the feasibility of surgical separation (Fig. 1). Both were intellectually normal, fluent in Persian/Farsi.

Abbreviations used in this paper: BOLD = blood oxygen level–dependent; fMR = functional magnetic resonance; IAP = intracarotid amobarbital procedure; ICA = internal carotid artery; IFG = inferior frontal gyrus; IPL = inferior parietal lobe; LI = laterality index; MFG = middle frontal gyrus; MTL = middle temporal lobe; ROI = region of interest; SFG = superior frontal gyrus; S/N = signal-to-noise; STL = superior temporal lobe.
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(mother tongue) and English, and university graduates. The right twin (Twin A) was right handed, whereas the left twin (Twin B) was left handed. Structural and morphological information had been obtained from computerized tomography, MR imaging, and angiography studies performed at another center in Singapore and one in Germany. These studies indicated that the twins had a single cranial cavity, within which were two anatomically intact brains, that is, each with two cerebral hemispheres, two cerebellar hemispheres, and separate brainstems. The temporal and parietal lobes on the apposed sides were compressed against each other and appeared to be mildly hypoplastic. The superior sagittal sinuses of each twin was fused into a common large venous sinus in the conjoined posterior third region.

Magnetic Resonance Imaging Data Acquisition. All imaging data were acquired on a 1.5-tesla MR imaging unit by using the quadrature body coil in the transmit and receive mode (NVi; GE Medical Systems, Milwaukee, WI) given that no standard head coil would have been able to accommodate the twins’ heads. We had to work toward a reasonable duration of imaging to minimize head movement, which would degrade image quality and affect data interpretation. Hence, the use of a body coil while minimizing the imaging time resulted in a necessary trade-off in the S/N ratio. Selection of the slice angle/orientation to avoid the echo planar imaging susceptibility artifacts usually encountered at the skull base was challenging, because of the tilted angle of fusion of the twins’ heads, which were not at the same anatomical location in the axial plane.

For the fMR imaging studies, a continuous T$_2^*$-weighted gradient-echo echo planar imaging sequence was used. Sixty volumes were acquired per task, with eight axial slices for each (TR 2000 msec; TE 40 msec; flip angle 90°; 8-mm slice thickness with a 2-mm gap; field of view 35 × 35 cm; 128 × 128 image matrix, covering both cerebral hemispheres).

Corresponding T$_1$-weighted MR anatomical images were acquired in the same slice plane. Additionally a three-dimensional anatomical volume of the whole brains was acquired using a spoiled gradient–recalled acquisition sequence with the following parameters: TR 10 msec, TE 4 msec, flip angle 15°, 116 slices, 2-mm slice thickness, field of view 35 × 35 cm, 256 × 256 image matrix.

Functional MR Imaging Tasks. Four cognitive tasks were performed to each twin individually and in the same order. The first consisted of a visual perception task that required looking at a flashing checkerboard sequence. Besides serving as a control task, it was also used to evaluate the twins’ primary visual areas, given that part of their fusion included the occipital lobes. This task was followed by three language tasks: a silent reading task and two picture-naming tasks. The first two language tasks were done in English and the last one in Persian. These tasks were expected to elicit activations in the major cortical areas expected to be activated by the language tasks: the MTL and STL around the Wernicke area plus the IPL, the IFG around the Broca area, and the MFG and SFG.

Data Analysis. Strong ghosting effects were cleaned up by using a masking procedure written in IDL, version 6.0 (Research System, Inc., Boulder, CO). Analysis and other preprocessing of the data were done using BrainVoyager 2000/QX (Brain Innovation B.V., Maastricht, The Netherlands), based on the general linear model. Data were corrected for slice-timing and motion, spatially smoothed with a gaussian kernel of 6 mm full width half-maximum, linear detrended and low pass–filtered at 2.8 seconds full width half-maximum. The BOLD response was modeled using a boxcar function and convolved with a standard hemodynamic response function. The t-tests were performed on a voxel-by-voxel basis, corrected for multiple comparisons, with a probability value less than 0.05 (t ≥ 5.5, df = 56).

The cerebral hemispheric dominance of task activation for each twin was calculated using the LI: (L − R)/(L + R). Left hemispheric language dominance was defined at an LI greater than 0.2, right hemispheric language dominance at an LI less than −0.2, and indeterminate or bilateral activation at an LI between −0.2 and 0.2, as previously reported. The complex neuroanatomy of the twins made it necessary to define broad and homologous brain ROIs in each hemisphere. Significantly activated voxels in these ROIs for each language task were included in the calculation of the LI for each twin. The ROIs consisted of the major cortical areas expected to be activated by the language tasks: the MTL and STL around the Wernicke area plus the IPL, the IFG around the Broca area, and the MFG and SFG.
Results of the Imaging Studies. Activations were considered to be significant if they met a threshold probability value less than 0.05 (t ≥ 5.5, df = 56), corrected for multiple comparisons. In Twin A, the English reading task activated mainly the left MTL/STL/IPL around the Wernicke area and a small cluster around the right IFG (Fig. 2). In Twin B, there was bilateral activation around the MTL/STL/IPL as well as in the left MFG/SFG. The picture-naming task in English activated in Twin A the left MTL/STL/IPL, the left IFG, and bilateral MFG/SFG. Twin B showed activation mainly in the bilateral MTL/STL/IPL (Fig. 3). The picture-naming task in Persian activated the left MTL/STL/IPL and bilateral MFG/SFG in Twin A, and the right MTL/STL/IPL, right IFG, and bilateral MFG/SFG in Twin B. The control task of visual perception elicited significant BOLD activation in both twins in the primary visual area. The visual association areas (precuneus and cuneus) were additionally activated in Twin A.

The global results of the three language tasks demonstrated strong left dominance for language in Twin A, with an overall LI of 0.86. Across the same tasks, Twin B’s results yielded an overall LI of 0.05, with more bilateral engagement, especially in the homologous MTL/STL/IPL region.

There was some obliteration of Twin B’s fMR imaging data in the inferior left portion of the brain due to the echo planar imaging distortions produced by the osseous skull base anatomy, paranasal sinuses, and mastoid air cells.

For each language task—all of which were twin-specific—a few spurious activations were noted in the opposite twin in whom no stimuli had been delivered during the course of the tests involving the sister. Most of these activations occurred in regions near strong signal gradients, such as in the area of the ventricles, paranasal sinuses, mastoid air cavities, and skull. Although the images were realigned to correct for motion, task-related movement in the sub-voxel range could still have induced these spurious activations. An examination of the time courses of the BOLD signal in these unexpectedly activated voxels revealed relatively noisy and noncanonical hemodynamic response functions. Additionally, the mean signal value in the voxels of these activations were one half to two thirds lower than that in the voxels of expected activations. Taken together, results of these investigations indicate that the occasional unexpected activations in the opposite twin were simply spurious and could be classified as movement-related artifacts. The twins did not have any anatomical or functional connections between them and had separate central nervous systems except for a posteriorly shared superior sagittal sinus.

Discussion

Language Laterality Findings and Handedness

Twin A, who was right handed, was clearly left lateralized for language, whereas results in the left-handed Twin B were considered to be bilateral or indeterminate. It is generally recognized that language lateralization and handedness are associated. The majority of healthy persons are left-hemisphere dominant for language function, with right-handed individuals being markedly stronger in terms of this left laterality in both healthy and clinical populations. Left-handed persons, however, have been reported to exhibit more bilateral or right hemisphere language-related activity compared with right-handed persons. The strong relation observed between handedness and language laterality indicates a genetic contribution.

Note, however, that results of twin studies have been interesting and sometimes conflicting. Data from a meta-
analysis of twin studies on handedness have revealed a higher proportion of left-handed individuals among twins compared with singletons, with monozygotic twins having greater intrapair concordance than dizygotic twins, thus implying a genetic influence in handedness. Authors of other large studies did not find a significant difference between the intrapair concordance of twin types, however. Comparatively few studies on language laterality in twins have been done. Data from two studies showed no significant concordance for language dominance in monozygotic twins regardless of handedness, whereas results from a recent study demonstrated significantly higher concordance for language laterality in the monozygotic twins with the same handedness than in those with discordant handedness.

Theories to explain the language laterality discordance in twins include late splitting of the embryo, which affects development of the typical asymmetry, pathological handedness and language laterality induced by birth complications (for example, injury to the left hemisphere) in twins compared with singletons and even the twinning process itself, which has been postulated to affect the regular evolution of asymmetry in the embryo. Laterality defects, such as heart situs reversal, have been noted in conjoined twins, although none has been observed in craniopagus. In the present case of craniopagus, we provide an example of monozygotic twins with discordant handedness and language lateralization.

Of course, there is the possibility that the twins’ handedness is a result of forced practicality rather than nature. It would certainly be more convenient for each twin to use habitually the hand on the outer side, which were indeed their announced dominant hands. Unfortunately, information on the original handedness of the twins during childhood was not available and hence we can only postulate the possibilities. Currently, there is no published data on handedness in craniopagus or any other type of conjoined twins. One wonders: if one or both twins’ handedness was altered or forced by practicality, did this alteration affect their language lateralization? To our knowledge, no literature exists on the effects of forced handedness. Nevertheless, an effect on language lateralization from forced handedness is probably unlikely given that functional and structural asymmetry appear from birth and remain stable throughout life unless there is injury to the dominant hemisphere, in which case a transfer of function to the nondominant hemisphere could occur. Hence, in the present case, we postulate that the twins’ original language dominance is as observed using fMR imaging studies.

Functional MR Conventional imaging equipment originally designed to accommodate one patient was adapted and tailored for the twins to permit adequate imaging coverage of a region consisting of two adult brains, while maintaining the diagnostic quality of the image data. The technical challenges included the use of a body coil to accommodate the two heads and the restriction on imaging time to avoid excessive movement artifacts. These strategies resulted in a necessary trade-off with S/N ratio. Furthermore, the automatic preimaging procedures of the imaging unit did not adequately calculate the center of the echoes in the echo planar imaging readouts, resulting in strong ghosting artifacts. To perform the rest of the analyses, these ghosting artifacts were removed using a simple masking procedure. Note, however, that the part of the signal present in these artifacts was lost at the same time, therefore resulting in a slight but additional reduction in S/N ratio.

![Functional MR images](image-url)
Because of the tilted angle of fusion of the twins' heads, which were not at the same anatomical location in the axial plane, there was difficulty in selecting the best slice angle/orientation to reduce the susceptibility distortions inherently encountered at the skull base during rapid echo planar imaging. These artifacts resulted in signal dropout at the left inferior frontal region in Twin B. This factor could have diminished the ability to detect task-related BOLD responses in Twin B’s left inferior frontal region, possibly resulting in a larger right-hemisphere bias in the calculation of the LI for Twin B. Nonetheless, there was sufficient quality in the rest of the images to permit satisfactory analyses.

The Wada Test

A traditional albeit invasive test for language hemispheric dominance is the IAP, or the Wada Test, which involves the intraarterial injection of amobarbital during cerebral angiography performed using a catheter. The results of an independent Wada test conducted at a separate examination indicated left dominance for language in both twins, although there was also minor language representation in the right hemisphere in Twin B (see Appendix for more details). These results concurred mainly with our fMR imaging data. Generally, results of language dominance tests with the aid of fMR imaging agree with those obtained using Wada testing and electrocortical stimulation, though there was also minor language representation in the right hemisphere in Twin B (see Appendix for more details). Although some differences have also been reported in 5 to 10% of the literature on these methods, including H.11,12,22,27,44-54, although some differences have also been reported in 5 to 10% of the literature on these methods, including H.11,12,22,27,44-54.

Presurgical Evaluation

Language mapping with the aid of fMR imaging as part of a large battery of tests for presurgical evaluation was important in the present case because the patients were adults who had mature nervous systems, and our aim was to minimize postsurgical morbidity and loss of function. Previous cases of craniopagus separation have only involved very young children with developing nervous systems, for whom the surgical considerations are rather different.10,24,25,52,53 Despite the experimental and practical difficulties with functional imaging in young children, children’s nervous systems demonstrate more plasticity than that in adults, thus potentially allowing for more functional reorganization following brain injury.11

In the present case of adult craniopagus, task-related fMR imaging provided useful information for surgical planning and presurgical counseling on the risks of possible postoperative deficits. In Twin A, who had evidence of language lateralization in the left hemisphere, it was important to preserve the integrity and function of this hemisphere, which lay apposed to the right hemisphere of Twin B; this fact was slightly less important in Twin B, who had bilateral hemispheric language function. Because surgical separation would involve working in the plane between the left hemisphere in Twin A and the right hemisphere in Twin B, any surgical trauma to Twin A’s left hemisphere would expose her to a higher risk of postoperative language deficits. It was important to convey this information to the twins so that they understood the risks of surgery and could give informed consent.

With regard to surgical planning, one critical element of the separation procedure was the creation of a second separate venous sinus drainage channel from the preexisting common (conjoined) posterior sagittal sinus. Given that this procedure would entail placement of a venous bypass graft, which carries the risk of thrombosis and subsequent venous infarction, it was considered more appropriate to place the graft on Twin B’s side of the common sinus. In this way, the integrity of the venous sinus system on Twin A’s side would be preserved and the risk to her left hemisphere would be reduced.

The twins were separated during surgery and both women died shortly thereafter.10,26 Further information regarding the surgical procedure and its outcome will be discussed in a subsequent paper.

Conclusions

Noninvasive fMR imaging has been used for the first time in the preoperative determination of eloquent brain areas in adult craniopagus. Regardless of the surgical outcome, the acquired data provided prognostic information that was useful in the presurgical counseling of the twins and guided surgical planning. The findings could also be of interest to current researchers of language laterality and handedness.

Appendix

Intracarotid Amobarbital Procedure

Method. The IAP was performed by two neurologists—one for each twin. The first neurologist stood at the right side of Twin A while the second stood at the left side of Twin B. The IAPs were performed at 30-minute intervals in the following order: right ICA in Twin B, left ICA in Twin A, left ICA in Twin B, and right ICA in Twin A. After each amobarbital injection during the period of transient hemiplegia in one twin, language function was assessed in both twins simultaneously by asking them to name, in English, a number of words and pictures presented to them. Once the effects of the amobarbital wore off, they were tested on memory of the items presented earlier to them.

Findings. Right ICA Injection in Twin B. There was left hemiparesis in Twin B following a right ICA injection. She was able to name seven of the eight items presented, making paraphasic errors while naming four. Twin B demonstrated no weakness or language dysfunction.

Left ICA Injection in Twin A. Right hemiplegia occurred in Twin A following the left ICA injection. She was able to name seven of the eight items presented, making paraphasic errors while naming four. Twin B demonstrated no weakness or language dysfunction.

Left ICA Injection in Twin B. Right hemiplegia occurred in Twin B following the left ICA injection. She was only able to name two of the eight objects presented and made paraphasic errors on naming both items. Twin A demonstrated no weakness or language dysfunction.

Right ICA Injection in Twin A. There was left hemiplegia but no weakness in Twin A following the right ICA injection. She was able to name five of the eight items presented with no paraphasic errors. Twin B had no weakness or language dysfunction.

Conclusions. Based on findings from the IAPs, both twins were left-hemisphere dominant for language. Note, however, that Twin B might have also had mild language representation in the right hemisphere given the one paraphasic error made in naming.
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References


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