Prevalence of Hippocampal Malrotation in a Population without Seizures

BACKGROUND AND PURPOSE: Hippocampal malrotation (HIMAL) is a failure of hippocampal inversion that occurs during normal fetal development and has been seen on MR imaging examinations of people with epilepsy, but it has not been studied in patients without epilepsy. We intended to evaluate the prevalence of HIMAL in MR imaging examinations of patients without seizures to better understand the significance of HIMAL in the population with seizure.

MATERIALS AND METHODS: A total of 497 MR imaging examinations with thin-section imaging through the temporal lobes of patients referred for conditions other than seizures were reviewed. The examinations were performed on 1.5T magnets. Sagittal T1-weighted and coronal T2-weighted images were used to evaluate each MR image for the distinctive features of HIMAL. As previously described in the literature, the criteria for HIMAL include unilateral involvement and incomplete rotation of a hippocampus that is normal in size and signal intensity but abnormally rounded in shape, with blurred inner structure. In addition, ipsilateral findings of an atypical collateral sulcus angle and atypical position and size of the fornix were noted. The corpus callosum is normal, and the temporal lobe remains normal in size, though the temporal horn may appear enlarged.

RESULTS: None of the patients’ examinations fulfilled all of the HIMAL criteria. Six studies satisfied 2 or more criteria, which included an abnormally rounded hippocampus and a vertical collateral sulcus. These HIMAL findings were all seen on the left. Fornical asymmetry was the most prevalent abnormality, with 289 patients manifesting a low position of 1 fornix.

CONCLUSIONS: Hippocampal malrotation is a rare finding in patients without seizures. HIMAL is therefore likely to be a pathologic finding.
tion was recruited from a consecutive series from each magnet. Sagittal T1-weighted spin-echo (SE) imaging (TR, 480 ms; TE, 13 ms; flip angle, 69°; section thickness, 5 mm; spacing, 6 mm; matrix, 256 × 256 or TR, 450 ms; TE, 14 ms; flip angle, 69°; section thickness, 4 mm; spacing, 5 mm; matrix, 256 × 256) and T2-weighted coronal SE imaging (TR, 5500 ms; TE, 110 ms; section thickness, 5 mm; spacing, 6 mm; matrix, 256 × 256 or TR, 3000 ms; TE, 80 ms; section thickness, 3 mm; spacing, 3.3 mm; matrix, 256 × 256) were used to evaluate each subject for the presence of distinctive features of HIMAL. The coronal images were perpendicular to the long axis of the hippocampus.

Each study was independently reviewed by 2 board certified radiologists, and 1 medical student who was trained to recognize the distinctive features of HIMAL. Any potential HIMAL case was then reviewed by an adjudicating senior CAQ (Certification of Added Qualification) certified neuroradiologist and a board certified neuroradiologist who had experience in evaluating patients with seizures. Retrospective chart review or consultation with the patients' primary care physicians was performed in these 6 patients with partial HIMAL features to verify that they do not have any history of seizures.

Statistical analysis with use of the Fisher exact test comparing our results (no HIMAL case in 497 patients referred for conditions other than seizures) with those of Barsi et al3 (32 HIMAL cases in 527 patients with seizures) was highly significant (P value of 4.19 × 10−10 with a 95% confidence interval). Of the 6 MR imaging studies with 2 or more HIMAL criteria, 1 demonstrated a low fornix and 5 demonstrated a normally positioned fornix. Of the 209 subjects with a normal fornix, 6 (2.9%) demonstrated 1 or more HIMAL criteria; of the 289 with a low fornix, 1 subject (0.35%) demonstrated additional HIMAL criteria.

Our cohort of patients had a female predominance that was not fully explained because there was no selection on the basis of sex.

**Discussion**

This retrospective review demonstrates that hippocampal malrotation is nearly nonexistent in patients referred for MR imaging for conditions other than seizures. However, there were limitations to our study. The prevalence of HIMAL reported by Barsi et al3 served as the reference point for our calculations because, to our knowledge, there is limited additional literature indicating the prevalence of HIMAL. We used a similar protocol to that of the study by Barsi et al3 and we used their list of the common imaging characteristics of HIMAL in our evaluation of HIMAL. In analyzing our data, we compared our observations with those of their study. Potential bias existed because we may have implemented the HIMAL criteria differently.

The study by Barsi et al3 does not provide information for patients who did not fulfill all of the HIMAL criteria. Therefore, the percentage of patients without HIMAL but with a low fornix is unknown. These data might further clarify the exact significance of the fornix position as a HIMAL criterion. Because a low fornix was prevalent in 58% of our patients without seizures and without HIMAL, we hypothesize that a low fornix might be a normal variant. A low fornix is not associated with any known neurologic sign or symptom. Additional research may elucidate whether a low-positioned fornix is pertinent to the HIMAL criteria vs a normal variant.

Because 2.9% of our subjects with a normally positioned fornix had 1 or more HIMAL criteria and 0.35% with an associated low fornix had 1 or more HIMAL criteria, it is plausible that a low fornix may be incidental.

The FEBSTAT study,4 a prospective multicenter study of febrile status epilepticus funded by the National Institutes of Health, examined the presence of hippocampal abnormalities on MR images of children with prolonged febrile seizures. In a
preliminary analysis of the early cases, HIMAL was found in 9 of 61 febrile status cases and in 3 of 56 control cases with more brief febrile seizures. All of these cases of HIMAL occurred on the left side. The previous findings, which will be confirmed in the larger cohort of 200 that FEBSTAT will ultimately recruit, suggest that HIMAL is a pathologic finding because it was found more commonly in the children with prolonged febrile seizures. Follow-up imaging of these children should help determine whether HIMAL predisposes them to temporal lobe epilepsy and mesial temporal sclerosis.

Our study did not address the effect of age on the rounded appearance of the hippocampus. Our purpose was not to conduct a longitudinal study of the normal hippocampus but, rather, to address the prevalence of HIMAL. A separate study would be required to assess how the hippocampus changes with age.

A similar study design sought to determine the presence of mesial temporal sclerosis on MR imaging examinations of patients without seizures. The study concluded that mesial temporal sclerosis is uncommon in the population without seizures and should prompt investigation of an underlying seizure disorder. In a likewise fashion, our study has shown that HIMAL is also uncommon in the population without seizures and should prompt investigation of an underlying disorder.

Conclusions

HIMAL is a rare finding in patients referred for MR imaging for conditions other than seizures. An imaging finding of HIMAL should therefore raise suspicion of an underlying potential for or the presence of a seizure disorder. Our study failed to demonstrate an association between HIMAL criteria and a low-lying fornix.

References

5. Lewis DV, Chan S, Bello JA, et al. HIMAL is a malformation that predisposes to prolonged febrile seizures: data from the FEBSTAT Study. Epilepsia 2006;47(Suppl 4):16