Subcortical heterotopic gray matter brain malformations
Classification study of 107 individuals

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Study objective and summary result
This study systematically examined the neuroimaging and clinical features of patients with subcortical heterotopia (SUBH), and it observed a broad spectrum of neuroimaging and clinical features.

What is known and what this paper adds
Research into malformations of cortical development (MCD) has led to the description of diverse MCD subtypes, including SUBH, which is rarely identified. This investigation clarifies the clinical spectrum associated with SUBH.

Participants and setting
The investigators reviewed data from 107 patients with SUBH who were identified by querying databases of patients with MCDs from Seattle, Rotterdam, Florence, and San Francisco.

Design, size, and duration
The investigators reviewed the available clinical and imaging data. All patients previously underwent brain MRI with T1-weighted and T2-weighted sequences, and the available scans were reviewed to classify the visible brain malformations.

Primary outcome measures
The primary outcomes were the patients’ clinical and neuroimaging characteristics.

Main results and the role of chance
Most of the patients had developmental and neurologic dysfunctions that included cognitive and motor deficits. Epilepsy was commonly observed. Many of the patients had brain malformations in addition to SUBH, such as abnormalities of the corpus callosum, brainstem, and cerebellum. Unilateral and bilateral distributions of brain malformations were both observed, but the brain was often asymmetrically affected. Genetic testing was not routinely performed, but the investigators concluded that the sporadic occurrence of the majority of SUBH and the consistent finding of brain asymmetries suggested that the patients’ features resulted from either postzygotic mutations or prenatal disruptive events.

Bias, confounding, and other reasons for caution
This investigation was conducted retrospectively and relied on incomplete data for its analyses.

Generalizability to other populations
The reliance on data from 4 cities in high-income countries may limit the generalizability of the study results.

Study funding/potential competing interests
This study received no funding. Some authors report receiving fellowships and grants from the European Molecular Biology Organization, the Dutch Society of Human Genetics, the Erasmus Medical Center, the Dutch government, the European Union, and the NIH. Go to Neurology.org/N for full disclosures.

Table
Frequencies of selected clinical features in the patients with available data

<table>
<thead>
<tr>
<th>Clinical feature</th>
<th>Cases reported out of patients with available data (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epilepsy</td>
<td>50/72 (69)</td>
</tr>
<tr>
<td>Delayed development/intellectual disability</td>
<td>55/68 (81)</td>
</tr>
<tr>
<td>Non-CNS malformations</td>
<td>32/69 (46)</td>
</tr>
<tr>
<td>Bilateral SUBH</td>
<td>67/107 (63)</td>
</tr>
<tr>
<td>Corpus callosum abnormalities</td>
<td>65/102 (64)</td>
</tr>
</tbody>
</table>

A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The authors of the full-length article and the journal editors edited and approved the final version.
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