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MR of the Cerebral Operculum: Abnormal Opercular Formation in Infants and Children

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PURPOSE: To evaluate abnormalities of the cerebral operculum in infants and children and to propose the embryogenic basis of abnormal opercular formation as determined from MR imaging findings. **METHODS:** Eighty-six infants and children who had abnormally wide interopercular distances and/or distorted opercular topography seen on MR images were studied retrospectively. Clinically, patients presented with tonal abnormalities, macrocephaly, microcephaly, seizures, developmental delay, cerebral palsy, or facial dysmorphism. The abnormal opercula were compared with developing opercula at different stages of gestation. **RESULTS:** Among the 86 infants and children, two categories of opercular abnormalities were identified: an underdeveloped operculum (n = 64) and a malformed operculum (n = 22). The malformed operculum was further classified into three subtypes: nonformation of the operculum with lissencephaly (n = 1, 1%), abnormal opercular formation with pachygyria (n = 11, 13%), and nonformation or abnormal formation of the operculum without pachygyria or lissencephaly (n = 10, 12%). Two subtypes of the underdeveloped operculum were identified: an open operculum without a normal insula (n = 6, 7%) and an open operculum with a normal insula (n = 58, 67%). The five subtypes of abnormal opercular configuration showed a range of maturity that was comparable to the developing operculum at different ages. **CONCLUSION:** Opercular anomalies appear to follow sequentially predetermined normal steps in development. Arrest in opercular development or malformation may occur after an initial insult. MR imaging is the method of choice by which to identify these abnormalities.

Index terms: Brain, abnormalities and anomalies; Brain, growth and development; Brain, magnetic resonance

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Structural development of the brain surface is similar to myelination of the cerebral white matter in that it is one of the major maturational processes of the human central nervous system that occur throughout fetal life and the early postnatal period, providing remarkable insight into the developmental milestones (1–3). Among the more dynamic changes in surface configuration are those that involve the lateral convexities of the cerebral hemispheres, in which the future operculum develops (3). The cerebral operculum—comprising parts of the frontal, temporal, and parietal lobes that override the insula—starts to develop by 20 to 22 weeks' gestation and proceeds in a well-defined and predetermined manner. Like the other developmental processes of the brain, development of the operculum (part of the cortical plate) can be affected by a variety of in utero insults that affect the immature cerebrum, resulting in a developmental arrest or malformation (4, 5). Because the operculum encompasses areas important for language and speech, auditory function, and secondary somatic sensory and motor function (6, 7), a developmental arrest or malformation of this vital

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area may cause significant impairment with developmental delays (8, 9).

The insula should be fully covered by the operculum at the time of full-term birth (3). Underdevelopment of the operculum, with an exposed insula, and malformation of the operculum, with or without normally formed insular gyri, can be recognized by computed tomography (8, 10). With magnetic resonance (MR) imaging, the brain can be delineated in vivo with multiple planes (11), thus providing a detailed surface configuration of both the normal and abnormal operculum. In this study, we evaluated the MR images of 172 abnormal opercula using previously established reference values of the interopercular distances and MR opercular topography (11). We then compared these abnormal opercular configurations with developing milestones of the fetal operculum at different stages of gestation so as to propose the possible embryogenic basis of abnormal opercular formation.

Materials and Methods

Subjects

MR images of the operculum of 53 infants and 33 children, ranging in age from 2 days to 14 years, were studied retrospectively. MR imaging was done during a period of 20 months (July 1992 to February 1994) at two institutions. Patients who were included in this study had interopercular distances greater than the normal values for infants or children, which had been established in a previous study (11), and malformed opercular configuration, in which normal topography could not be identified on axial, sagittal, or coronal MR images. All patients had irregular neurologic signs, including abnormal tonicity, microcephaly, macrocephaly, seizures, developmental delay, dysmorphism, and cerebral palsy. None of the patients had MR evidence of tumor, hemorrhage in the cerebral hemisphere, infarcts, brain atrophy, and/or enlargement of the subarachnoid spaces.

Imaging Technique

MR images were obtained with two 1.5-T scanners. The imaging sequences consisted of spin-echo T1-weighted, 500–600/15–40/1–2 (repetition time/echo time/excitations), axial and sagittal images with 3-mm to 5-mm section thickness and T2-weighted, 2800–3000/90–120/1–2, axial and coronal images with 5-mm section thickness. Additional coronal T1-weighted images were obtained occasionally for further information. The matrix size was 256 $\times$ 256 in the sagittal plane and 160 to 192 $\times$ 256 in the axial or coronal planes; the field of view varied from 20 to 25 cm depending on the patient's head size.

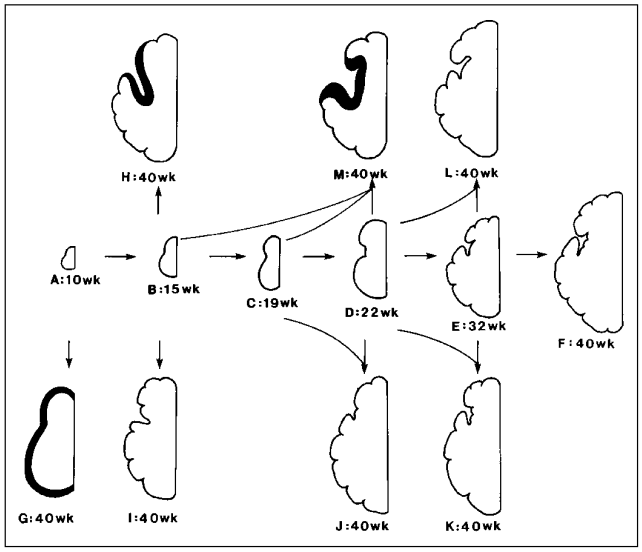


Fig 1. Proposed embryogenic development of normal and abnormal opercular formation.

A through F show normal opercular development from 10 to 40 weeks' gestation on axial views. The primary sylvian fissure becomes grossly visible at 14 to 16 weeks (*B*). The indented insula is formed at about 19 to 20 weeks (*C* and *D*). The bulk of hemispheric growth starts by 20 to 22 weeks at the parietal and temporal lobes and continues to override the insula until full-term birth, when the insula is completely embedded by operculum (*F*).

In *G* (type 1 abnormality), the operculum is not formed and the cortex is thick, resulting in an abnormal configuration at the lateral convexity similar to the early fetal brain at the 10th to 15th week of gestation, a condition called *lissencephaly*.

In *H* and *M* (type 2 abnormality), the operculum is malformed with focal or diffuse pachygyria. The insula and circular sulcus are frequently not well developed in this type, indicating an opercular developmental milestone of no more than 22 weeks' gestation.

Type 3 abnormalities (*I*), which probably occur during the same period as type 2, have broad gyri and sulci but the insula is not formed to continue the normal opercular formation.

In type 4 abnormalities (*J* and *L*), the operculum, particularly the frontal lobe, is underdeveloped, resulting in a wide-open operculum with insula exposed. The insular gyri, which should be recognized after 34 weeks, are not well formed in this type.

In type 5 abnormality (*K*), the operculum is open and the insular gyri develop normally. This is the most common type.

Imaging Interpretation

Underdevelopment of the operculum (an open operculum) was defined as an increased distance ($>$4.5 mm in infants and $>$3.5 mm in children) between the posteroinferior border of the inferior frontal gyrus and the superoanterior border of the temporal lobe (anterior open operculum) on sagittal and axial images or an increased distance ($>$1.8 mm in infants and $>$0.5 mm in children) between the inferior border of the parietal operculum and the superior border of the temporal operculum (posterior open operculum) on sagittal or coronal images. The major surface landmarks of the cerebral operculum and the reference values for normal interopercular distances in infants and children have been reported in a previous study (11).

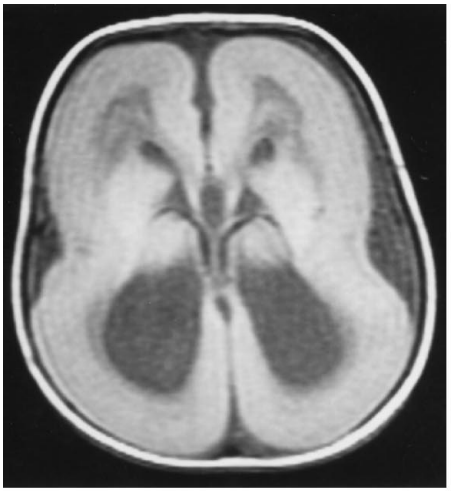
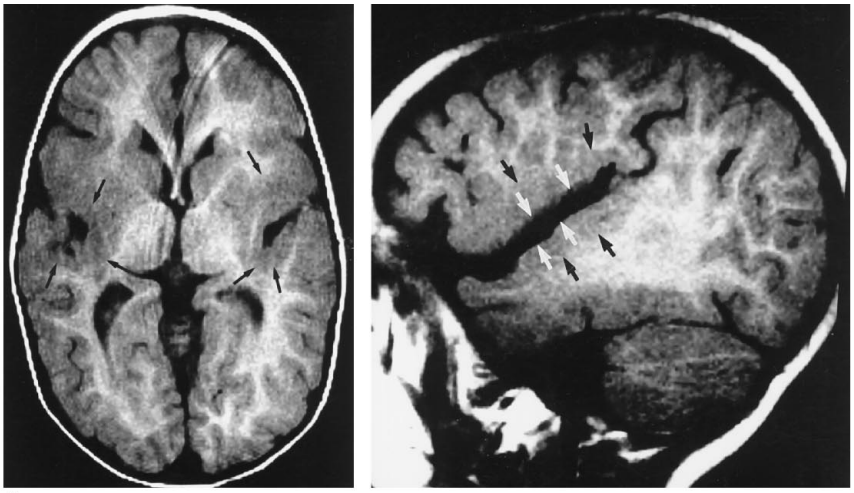


Fig 2. Type 1 abnormality of the operculum in a 2-month-old girl with Miller-Dieker syndrome. Axial T1-weighted (600/20/2) MR image shows complete absence of opercular formation with lissencephaly.

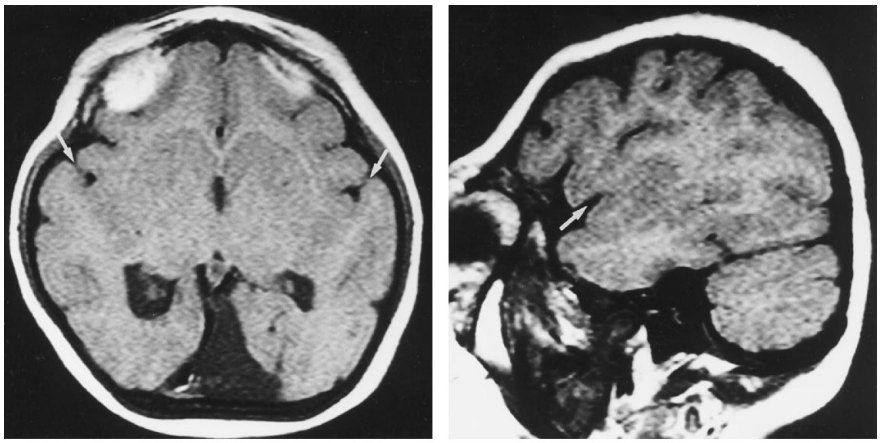


A B

Fig 3. Type 2 abnormality of the operculum in a 16-year-old boy who had marked developmental delay and hypotonia.

A, Axial T1-weighted (600/20/1) MR image shows vertically oriented sylvian fissures lined with abnormally thick cortex (*arrows*). The insula and circular sulcus are not formed. Also noted are the heterotopia over the frontal subependymal regions anterior to the caudate nuclei and along the bodies of lateral ventricles (not shown).

B, Lateral sagittal T1-weighted MR image shows the deep sylvian fissure (*white arrows*) without the insula. The thick lining of the cortex represents pachygyria (*black arrows*).



A B

Fig 4. Type 3, nonformation of the operculum, in a 32-month-old girl who had microcephaly and delay in language development. Clinical diagnosis was fetal alcohol syndrome. Axial and lateral sagittal T1-weighted (667/16/2) MR images show simple convolution of cerebral gyri. The sylvian fissure is shallow (*arrows*), and the insula has not been formed.

Abnormal opercular formation was defined as a deformed operculum in which only part of the insula and circular sulcus could be identified and part or all of the opercular area might contain abnormal sulci or gyri. Nonformation of the operculum was defined as the absence of a normal insula and circular sulcus on axial, coronal, and sagittal MR images. The MR studies were interpreted by two neuroradiologists without knowledge of the patients' clinical status. Subjects were categorized into two groups: those with an underdeveloped operculum and those with a malformed operculum. Each opercular abnormality was compared with normally developing opercula in fetuses of 10 to 40 weeks' gestational age as represented by autopsy specimens described by Larroche (3) and by MR imaging findings published by Mintz et al (12) and Hansen et al (13).

Results

Among the 86 patients, 64 had an underdeveloped cerebral operculum and 22 had a malformed cerebral operculum. We found three distinct subtypes of abnormal opercula: type 1 (Fig 1G), nonformation of the operculum with lissencephaly (1 case, 1%) (Fig 2); type 2 (Fig 1H

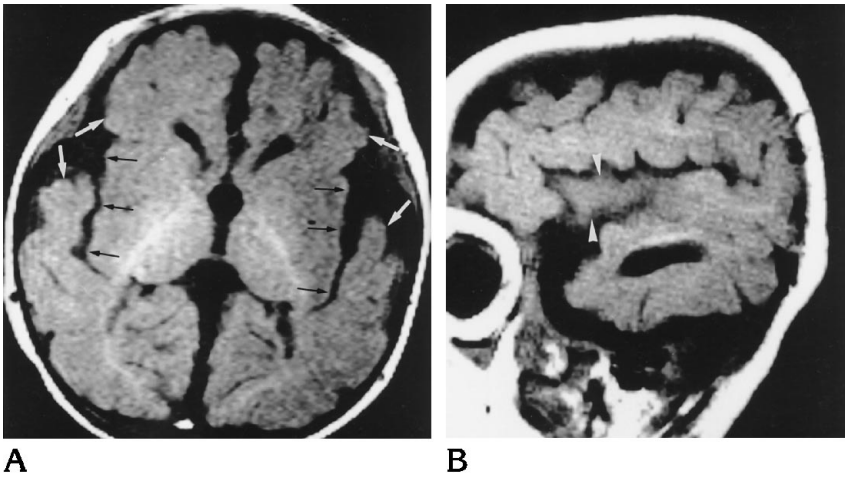


Fig 5. Type 4, underdeveloped operculum, in a 6-month-old boy who had multiple congenital anomalies.

A, Axial T1-weighed (600/15/1) MR image shows marked underdevelopment of the frontal and temporal opercula (*white arrows*) with exposure of insula. The insular surface is smooth (*black arrows*), with loss of undulating appearance, which should be recognized in normal insular gyration on cross-sectional view. The T2-weighted images (not shown) revealed no pachygyria or migrational disorders in the brain.

B, Lateral T1-weighted (600/15/1) MR image shows exposed insula with smooth surface (*arrowheads*).

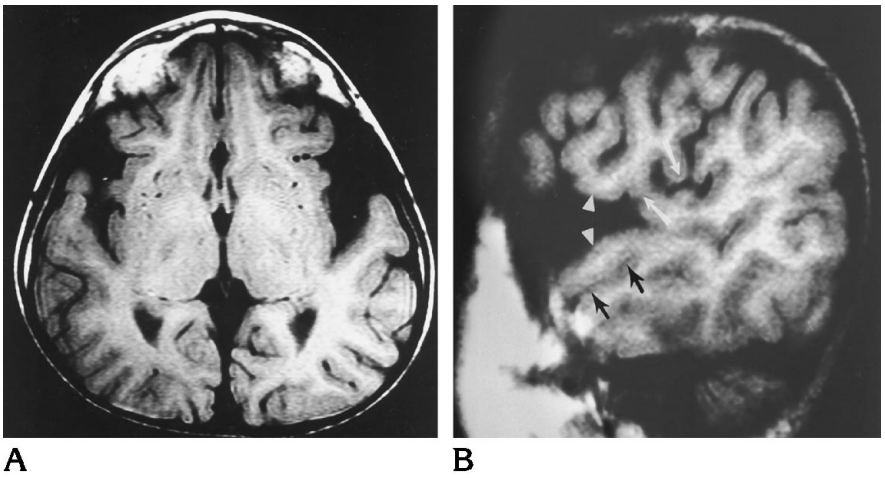


Fig 6. Type 5, underdeveloped operculum, in a 4-year-old boy with speech and language development close to that of a normal 15-month-old.

A, Axial T1-weighted (667/16/2) MR image shows marked widening of bilateral sylvian fissures (open operculum) with exposure of insula.

B, The most lateral sagittal T1-weighted MR image shows opercular opening (*arrowheads*). Also present is the underdeveloped superior temporal sulcus (*black arrows*), which ends posteriorly opposite the inferior precentral sulcus (*white arrows*). The normal posterior extent of the superior temporal sulcus should be beyond the posterior end of the sylvian fissure.

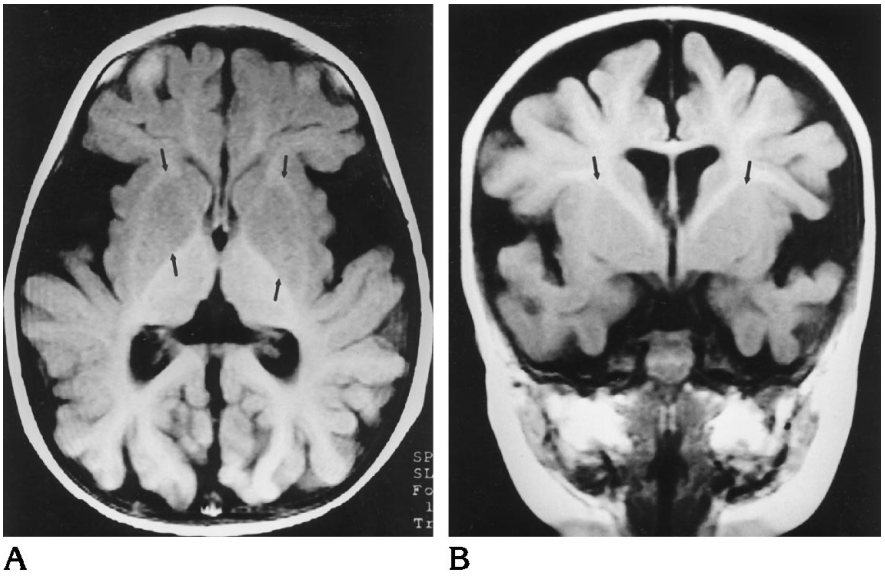


Fig 7. Type 1 glutaric aciduria. Axial and coronal T1-weighted (500/15/1) MR images show marked underdeveloped operculum with exposure of insula. The basal ganglia are of low signal intensity (*arrows*), characteristic of this disease.

Types of abnormal opercular formation as determined by MR findings in 86 infants and children

Type	No. of Patients (%)	No. of Abnormal Opercula				Clinical Signs	Underlying Diseases	Associated Cerebral Anomalies
		R Anterior Operculum	R Posterior Operculum	L Anterior Operculum	L Posterior Operculum			
1	1 (1)	1	1	1	1	Hypotonia (n = 1)	Lissencephaly (n = 1)	Corpus callosum dysgenesis (n = 1)
						Microcephaly (n = 1)		Lissencephaly (n = 1)
						Dysmorphism (n = 1)		
2	11 (13)	11	11	9	9	Hypotonia (n = 1)	Pachygyria (n = 8)	Heterotopia (n = 1)
						Macrocephaly (n = 1)		Corpus callosum dysgenesis (n = 3)
						Microcephaly (n = 3)		Pachygyria (n = 8)
						Seizure (n = 6)		
						Developmental delay (n = 8)		
3	10 (12)	9	9	10	10	Microcephaly (n = 1)	Holoprosencephaly (n = 6)	Heterotopia (n = 1)
						Seizure (n = 2)	Fetal alcohol syndrome (n = 2)	Corpus callosum dysgenesis (n = 3)
						Cerebral palsy (n = 1)	Schizencephaly (n = 1)	Holoprosencephaly (n = 6)
						Developmental delay (n = 8)		Posterior fossa anomaly (n = 1)
						Dysmorphism (n = 4)		Schizencephaly (n = 1)
4	6 (7)	5	5	6	6	Microcephaly (n = 4)	Treacher-Collins syndrome (n = 1)	Heterotopia (n = 1)
						Hypotonia (n = 2)	Multiple congenital anomalies (n = 1)	Corpus callosum agenesis (n = 1)
						Seizure (n = 3)	Pompe disease (n = 1)	Pachygyria (n = 1)
						Dysmorphism (n = 2)		
5	58 (67)	49	17	55	18	Abnormal tonicity (n = 12)	Canavan diseases (n = 1)	None
						Macrocephaly (n = 7)	Soto syndrome (n = 1)	
						Microcephaly (n = 7)	Glutaric aciduria (n = 2)	
						Seizure (n = 33)	Lactic acidosis (n = 1)	
						Developmental delay (n = 19)	Cytochrome oxidase deficiency (n = 1)	
						Down syndrome (n = 2)		
						Dysmorphism (n = 3)	Polycystic kidney (n = 1)	

and M), abnormal opercular formation with pachygyria (11 cases, 13%) (Fig 3); and type 3 (Fig 1I), nonformation or abnormal formation of the operculum without pachygyria or lissencephaly (10 cases, 12%) (Fig 4). Two subtypes of the underdeveloped operculum were identified: type 4 (Fig 1J and L), displaying increased interopercular distance (open operculum) with marked hypoplasia of the frontal operculum and an abnormal insula (6 cases, 7%) (Fig 5); and type 5, displaying an open operculum and a normal insula (58 cases, 67%) (Fig 6).

In comparing the morphology of malformed opercula with that of the normally developing operculum at different gestational ages, we found that the type 1 operculum was close in configuration to the fetal operculum at the 10th to 19th week of gestation (ie, no portion of the lateral convexity structure in type 1 was developed beyond that seen at 19 weeks' gestation), indicating a developmental arrest of the cortical plate before the normal operculum could be formed (Fig 1). Type 2 and type 3 malformations, in which the operculum has a primitive, shallow sylvian fissure without a normal insula and circular sulcus, indicate that the arrested or malformed operculum occurred before the 19th week of gestation, as there was no evidence of normal developmental opercular elements present beyond the 19th week of gestation. Two cases of type 2 anomaly had unilateral involvement, whereas the others were all bilateral. In type 4, the underdeveloped operculum, together with the immature insula, paralleled the opercular configuration found in the fetal brain between the 19th and 32nd week of gestation. The fifth type of operculum had a normal-appearing insula and an underdeveloped operculum, consistent with the developing operculum found after 32 weeks of gestation.

The five types of abnormal opercula appear to represent opercular formation consistent with arrested development at different stages of brain development, when different portions of the operculum have formed. The patients' clinical signs, known underlying diseases, associated cerebral anomalies, and various types of abnormal opercula are summarized in the Table.

Discussion

Development of the cerebral operculum is one of the major expressions of the functional maturity of the brain that demands several orderly predetermined steps. Until 14 to 16 weeks' gestation, the primordial cerebral hemispheres are smooth, similar to those of the lissencephalic mammals. The primary fissure, or sulcus, the earliest to appear, at about 14 to 16 weeks' gestation, is the circular sulcus of the insula (the sylvian fissure) on the ventrolateral wall of the hemisphere (1, 14). At approximately the same period, waves of migrating neurons coursing from the germinative zone at the ventricular surface to the cortical plate at the brain's surface form the future six-layered neocortex by 6 months of gestation (15). By 20 weeks' gestation, the cerebral hemispheres start to grow more rapidly at the primitive parietal and temporal lobes around the posterior part of the insula, and the frontal lobe begins to lag in growth. This discrepancy in the gain of the surface and bulk of individual lobes precipitates earlier development of the posterior operculum. The indented smooth insular cortex and circular sulcus (periinsular sulcus), which can be recognized by 19 to 22 weeks' gestation, are finally engulfed and overridden by the enlarged parietal, temporal, and frontal opercula from posterior to anterior. The anterior portion of the insula remains exposed until full-term gestation, and the insular gyri can be recognized after 32 to 34 weeks' gestation (1). It appears that any insult or genetic antecedent may influence the sequential steps of normal opercular formation and result in developmental arrest or malformation, even while certain developing milestones are achieved. The stage at which the developing operculum becomes arrested or malformed does not necessarily reflect the timing of an in utero insult to the brain. An early insult may lead to an early developmental arrest of the operculum, or, as an alternative, exert persistent influence on the brain so that the operculum becomes affected at a later gestational age. The causes of abnormal opercular formation and the timing of the insult are difficult to determine, like delayed myelination of the white matter. An abnormal operculum may reflect the stage of cerebral development at which the operculum became deranged.

The results of our study show five distinct types of abnormal opercula. In types 1, 2, and 3, the spectrum of abnormality is from complete absence to malformation of the operculum. Type 1 and type 2 opercular abnormalities fall into the category of neuronal migratory dis-

orders, characterized by a thick cortex and broad and smooth gyri. The operculum is basically not formed or is incompletely developed, with only shallow sylvian fissures remaining in the insular regions, giving an appearance close to that of a hemisphere at 10 to 19 weeks' gestation, a time when the indentation of the insula and bulky growth of the operculum have not yet begun. The association of abnormal opercular formation with disorders of neuronal migration has been reported by many investigators (10, 16–18). A recent report described 31 cases of congenital bilateral perisylvian syndrome with MR findings of bilateral perisylvian and perirolandic cortical thickening with exposure of the insula (19). The abnormally thick cortices were confirmed histologically to be polymicrogyria in two of those 31 cases. Barkovich and Kjos (18) described 36 patients with focal or diffuse cortical abnormalities that ranged from a normal to an increased cortical thickness and an irregular, bumpy gyral pattern with shallow sulci, which they called "cortical dysplasia." Some of their patients did have opercular involvement, as evidenced by the figures and the photographs of the autopsy specimens in their article. Histopathologic confirmation was available in four of their cases, and all showed polymicrogyria.

As mentioned above, migration of neuroblasts begins about 2 weeks before the appearance of the insula and its subsequent opercular formation, and is complete at 6 months' gestation, almost 3 months before opercular formation is complete. The question arises of whether the waves of migratory neurons arriving at the cortical plate induce opercular formation. We have seen several cases of focal pachygyria or polymicrogyria at the opercular region with complete formation of the operculum and insula. Moreover, there are situations in which nonformation or incomplete opercular formation occurs without agyria or pachygyria in the sylvian regions. This is exactly what we found in type 3 opercular abnormalities, in which there was an absence of the operculum and insula as well as a well-formed cortex and sulcus over the lateral convexities of the hemispheres. Thus, the unformed or malformed operculum might have been caused by multiple factors, not necessarily by a neuronal migratory disorder alone. In our study, for example, two patients with fetal alcohol syndrome and six with holoprosencephaly were totally lacking opercula, indicating that alcohol and genetic factors might influence opercular development in the first trimester.

Type 4 and type 5 opercular abnormalities might be pathogenetically different from the first 3 types of abnormalities, because they have recognizable insular lobes, a circular sulcus, and temporal and frontoparietal opercula, which indicate a later onset of abnormal opercular formation. The insular lobe is particularly worth mentioning in type 4 abnormalities. The normal insula encompasses several vertically oriented gyri, including short insular gyri anteriorly and long insular gyri posteriorly, both of which can be recognized after 32 to 34 weeks' gestation (1). In our series, absent or abnormal insular gyri were always seen in association with abnormal opercular formation. Conversely, we have not seen any insular gyral abnormality coexisting with normal opercular formation. The insula, per se, has been connected with speech and language functions (20, 21), because, anatomically, the arcuate fibers that connect the motor and sensory language centers traverse the insular subcortical region. So the insula should belong to a part of the operculum, both functionally and embryologically.

Opercular abnormalities may be caused by genetic factors, as the influences on the developing cerebral operculum are present from the time of fertilization, and changes may begin before opercular formation is initiated, as in Miller-Dieker syndrome (17), or later after most of the components of the operculum are formed, as in glutaric aciduria type 1 (22, 23) (Fig 7), Soto syndrome (24), Down syndrome (4), and nonsyndromic microencephaly (25).

In our study, most of the patients with type 5 abnormalities (50 of 58) did not have obvious underlying diseases. The underdeveloped operculum with exposed insula, which is normally seen in premature brains, is most likely due to arrested or delayed opercular formation after 34 weeks' gestation. A longitudinal study to follow up these patients with MR imaging and neurologic examination might help to elucidate the hypothesis that patients with type 5 delayed opercular formation may, as with delayed myelination, eventually acquire a fully formed operculum with concomitant improvement in clinical signs, particularly the development of speech and language.

Associated cerebral anomalies were high among patients with type 1 to type 4 opercular

anomalies (33 of 22). Among these, neuronal migratory disorders were the most frequent (14 of 33), followed by dysgenesis of the corpus callosum (see Table). Patients with type 5 abnormalities had no other associated cerebral anomaly. The most common sign in the 86 infants and children was seizure (45 [35%] of 130 signs), followed by developmental delay (28 [22%] of 130 signs). Among the 28 patients with developmental delay, 18 had clinical evidence of delay in speech and language development. The clinical severity did not correlate well with the MR findings regarding the degree of opercular abnormality. Previous reports have shown that although destruction of the opercula in the immature brain may be associated with abnormalities in speech, the plasticity of the developing brain may enable a reorganization of its hemispheric specialization, providing an alternative area for speech function (26, 27). It seems that a malformed operculum is not a prerequisite of abnormal speech and language development. Other factors, such as associated anomalies and underlying diseases of the brain, may also play a role in clinical symptomatology. In type 5 abnormalities, the connection between clinical signs and an underdeveloped operculum seems to be more direct, as no underlying diseases or associated brain anomalies were found. Again, we emphasize that a long-term follow-up of these patients should be the key to making clear the clinical delay relative to the underdevelopment of the operculum. A recent study by Kuzniecky et al (19) described a more discrete syndrome, including developmental delay, variable cognitive deficits, prominent cortical pseudobulbar signs, and variable pyramidal signs, in 31 patients with probable bilateral perisylvian polymicrogyria. The bilateral perisylvian syndrome in their cases is, we believe, an example of type 2 opercular abnormality. One limitation in our cases is that the association between delayed speech and language development and opercular abnormality was not evaluated comprehensively, partly because of the young age of our patients (54% were younger than 11 months old). To evaluate and follow up the development of speech and language in these patients, we are currently conducting a standardized psychometric evaluation of several patients in this group, including those with both normal and abnormal opercular formation.

In conclusion, our study has revealed five types of abnormal opercula, which reflect a range of milestone achievements in opercular formation. The opercular anomalies might indicate that development of the operculum may become arrested at any stage of gestation, from 15 weeks to birth, after the initial insult. The causes of these anomalies and their relationship to the clinical symptoms are best explained by multiple factors. MR imaging is the method of choice for identifying and following up these abnormalities.

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