Mesial Frontal Epilepsy

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Summary: The mesiofrontal cortex comprises a number of distinct anatomic and functional areas. Structural lesions and cortical dysgenesis are recognized causes of mesial frontal epilepsy, but a specific gene defect may also be important, as seen in some forms of familial frontal lobe epilepsy. The predominant seizure manifestations, which are not necessarily strictly correlated with a specific ictal onset zone, are absence, hypomotor, and postural tonic seizures. Other seizure types also occur. The task of localization of the epileptogenic zone can be challenging, whether EEG or imaging methods are used. Successful localization can lead to a rewarding outcome after epilepsy surgery, particularly in those with an imaged lesion. Key Words: Mesial frontal epilepsy—Cingulate gyrus—Supplementary motor area—Absence seizure—Hypermotor seizure—Postural tonic seizure—Epilepsy surgery.

FUNCTIONAL ANATOMY

The frontal lobe is the largest lobe in the brain, accounting for one-third to one-half of total brain volume and weight. On the medial surface, the most important landmark is the cingulate sulcus (Fig. 1). This runs as an inverted “C” following the contour of the corpus callosum. Starting at the region opposite the lamina terminalis below the rostrum of the corpus callosum is the subcallosal area. This merges with the anteriormost extent of the cingulate gyrus, the long band of cortex lying between the callosal and cingulate sulci. The cingulate gyrus curves posteriorly beyond the confines of the frontal lobe with its posterior portion in the parietal lobe, and continues around the splenium of the corpus callosum to become continuous with the parahippocampal gyrus. As the cingulate sulcus is followed posteriorly, it turns upwards into the marginal ramus and reaches the superior convexity. The central sulcus indents the superior surface of the brain anterior to the marginal ramus, thus defining the pre- and postcentral parts of the paracentral lobule. The paracentral lobule is limited anteriorly by the paracentral sulcus, a short ascending sulcus arising from the cingulate sulcus.

The medial frontal gyrus situated in front of the paracentral lobule and beyond the cingulate gyrus is extensive and is marked by many irregular gyriations. It can also be considered the medial surface of the first frontal convolution. Traditional cytoarchitectonics have further subdivided this anterior frontal region. The frontal pole refers to the anterior most portion of the frontal lobe, but there is little consensus on how far back this extends. One or more curved sulci are seen anterior and inferior to the cingulate sulcus, called the superior and inferior rostral sulci. The most inferior band of medial frontal cortex is contiguous with the orbital surface of the frontal lobe and the various orbital gyri, and can be regarded as part of the orbitofrontal cortex.

The functional areas on the medial frontal surface that have been best studied and defined are the anterior cingulate cortex and the supplementary motor area (SMA). The anterior cingulate cortex comprises cytoarchitectonic area 24, and functionally includes area 32, which is immediately dorsal, and subcallosal area 25 (1,2). It has the pattern of frontal agranular cortex with prominent layer V neurons. Afferent connections are predominant from the anterior, dorsomedial, midline, and intralaminar thalamic nuclei, and efferent projections are widespread to the primary motor cortex, dorsal and ventral striatum, the amygdala, thalamus, and periaqueductal gray in midbrain tegmentum. Stimulation studies evoke autonomic, visceromotor, or affective sensations, and simple to complex movement patterns (3). Motor functions found in the midportion of cingulate gyrus probably overlap with those of the supplementary motor area. Lesions of the anterior cingulate cortex produce affective and motor neglect, clinically apparent as apathy and akinetic mutism, and can lead to relief of chronic pain and obsessive compulsions (1). The posterior cingulate cortex has dif-
different cytoarchitectonics and connectivity and appears to participate more in visuospatial and memory functions (4).

The supplementary motor (and sensory) area, or supplementary sensorimotor area (SSMA), is best viewed as a functional rather than a strictly anatomically defined region. It is situated around and contiguous with the primary motor area for the lower limbs that occupies the precentral part of the paracentral lobule, and extends about 4–5 cm along the medial frontal gyrus. It includes all or most of the Brodmann medial area 6, and possibly parts of medial area 8 (5,6). A somatotopic organization has now been established in the human (7,8) as in the primate brain, in confirmation of Penfield’s model (Fig. 2). Most anteriorly is a supplementary eye field, probably in the medial portion of area 8. Motor representations for the upper limbs precede those for the lower limbs. The supplementary sensory areas are most posteriorly situated in the medioparietal cortex. The inferior limit of this functional area is variable and may overlap with and extend into the cingulate gyrus. Superiorly, it can extend to the convexity of the superior frontal gyrus. Afferent connections derive from thalamic nuclei ventralis anterior and lateralis and from the dorsomedial nucleus. Projections are found to the putamen, thalamus, pontine nuclei, and the spinal cord (5,9). There are also extensive reciprocal connections to many cortical areas. Cortical stimulation produces proximal, segmental, unilateral or bilateral, tonic postural movements as well as a range of somatic sensations. Lesions of the SMA can cause acute mutism, particularly in the speech dominant hemisphere, and contralateral or bilateral weakness that frequently resolve (see below).

The remaining anterior mesial frontal cortex comprises Brodmann’s areas 9 to 12 and is considered to be a part of the prefrontal cortex. There are extensive afferent and reciprocal connections to the dorsomedial thalamic nucleus and efferent projections to other cortical areas.

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areas, the basal ganglia, hypothalamus, and periaqueductal gray in the midbrain tegmentum.

All areas of the mesial frontal cortex have extensive connections with the opposite hemisphere via callosal commissural fibers and with other cortical areas via arcuate fibers. The SMA have relatively dense callosal connections compared to the primary motor cortex. Single shock stimulation studies (10) evoked shorter transcallosal latencies on the order of 10 ms between homologous SMA sites compared with longer latencies of 30-40 ms between homologous sites.

PATHOGENESIS

Knowledge of the pathologic substrate of frontal lobe epilepsy is strongly biased toward material obtained at epilepsy surgery and toward imaged lesions. Of 100 patients with frontal lobe epilepsy treated surgically at the Hopital St. Anne, Paris (11), only 7% had a brain tumor, and 15% each were attributed to encephalitis, head trauma, and diverse causes, 18% to neonatal anoxia, while 37% were of unknown origins. In the nontumoral Montreal series of 40 patients with "pure" frontal epilepsy who became seizure-free after surgery (12), and in a later compilation of up to 187 surgical specimens taken from the frontal lobe at the time of epilepsy surgery (13), the most common pathologic diagnosis was that of meningocerebral cicatrix (50%, 33% respectively in the two series), followed by gliosis (33%, 33%), and cortical dysgenesis (7.5%, 15.5%). The frequency of tumors in frontal lobe epilepsy treated surgically is probably a good deal higher than the figures above. In a group of 18 patients with SMA epilepsy treated surgically, seven had a tumor, five had evidence of cortical dysgenesis, and three exhibited changes of encephalomalacia (14). Head trauma much more commonly damages the anterior polar or orbitofrontal regions of the frontal lobe rather than its medial surfaces. As cerebral imaging techniques advance, small areas of cortical dysgenesis are increasingly recognized in patients with partial epilepsy (15).

Until the recent definition of familial forms of temporal and frontal lobe epilepsies with autosomal dominant patterns of inheritance, it has been assumed that partial epilepsies persisting into adulthood are usually symptomatic in nature. Although well recognized, the benign partial epilepsies of childhood are conceived of as idiopathic localization-related epilepsy syndromes unique to childhood, which run a benign course with frequent remission later in life. A benign frontal lobe epilepsy of childhood had been proposed (16), akin to benign childhood epilepsy with centrotemporal spikes. More recently, children with seizure characteristics similar to those of SMA epilepsy (17), or of suspected medial frontal origin (18) have been described. The affected children exhibited a relatively benign clinical course, and a positive family history of epilepsy was common. They very likely represent the early presentation of autosomal dominant frontal lobe epilepsy (19,20). In affected families, clinical seizure semiology is stereotyped, with features to be discussed below, that are strongly suggestive of seizures of mesial frontal origin. Scalp ictal EEGs have been difficult to localize or are obscured by artifacts. Intercital PET and SPECT studies confirmed regional hypometabolism or hypoperfusion, while ictal SPECT showed regional hyperperfusion involving mesial frontal cortex, with varying degrees of involvement of frontopolar and parasagittal regions (21). Onset is usually before the age of 20, and nocturnal seizures predominate. The gene for autosomal dominant nocturnal frontal lobe epilepsy in a large Australian kindred has been reported to be mapped to chromosome 20q, with the gene defect found to be a missense mutation at codon 248 in the gene for the α4-subunit of the neuronal nicotinic acetylcholine receptor (22). However, not all families with this syndrome share the same genetic defect.

CLINICAL MANIFESTATIONS

There are several ways in which a set of seizure phenomena can be recognized to correlate with a site of seizure onset, and with the mesiofrontal cortex in particular. One "gold standard" has been to analyze seizure semiology in patients who have become completely sei-
Intracranial EEG, remain strictly within that stated structure or lobe, when the seizure discharge, as defined by brain wave recruitment by the seizure discharge, it does not talk of seizure semiology as pertaining to a certain more often the rule than not. Even if different parts of the brain necessarily "speak with equal loudness" during a seizure, and some can remain "silent." This logic also fails to take into account that a set of symptoms and signs, even if a result of propagation, provided that they are organized and not random or infinitely variable, can still lead us back to a site or a small range of sites of seizure origin. In fact, it should be recognized that in general there are several preferred patterns of seizure propagation from each of the main epileptogenic zones (35).

Finally, with the knowledge gleaned by the post fact analysis of seizure semiology based on anatomic information of the epileptogenic zone, one can test whether certain groupings or sequences of ictal symptoms and signs correlate with sites of seizure onset. One such method is cluster analysis, initially employed for seizures of temporal lobe origin (36,37), and, more recently, in fronto lobe epilepsy (3,38). One problem in this type of analysis, is that a predetermined set of symptoms and signs have to be recognized, hopefully appropriate to the seizures under study. Second, the analysis will be unsuccessful in recognizing a correlation unless a sufficient number of examples from different sites are available in the sample.

With these provisos, it appears that mesial frontal epilepsy most commonly finds expression in one or more of three clinical seizure types: absence, hypermotor, and postural tonic seizures. Other seizure types, such as ursive or psychomotor seizures, are not precluded but occur less frequently. All seizure types can progress to secondarily generalized tonic–clonic seizures. Furthermore, the different seizure types may sometimes blend into each other or may coexist in the same patient. These observations support the notion that more than one seizure type can arise from a given brain region. It is uncertain whether this is because of our still rudimentary ability to precisely localize the epileptogenic zone and correlate it with its functional anatomy or because seizure expression is indeed a function of one of a number of potential pathways of propagation from the site of seizure origin. This point of view is somewhat different from the anatomically constrained model proposed by the Commission on Classification and Terminology (39), in which each brain region is correlated with its own seizure type. Rather, it is proposed that a number of seizure types may be found in frontal lobe epilepsy, as in any other localization-related epilepsy, based on the preferential activation of one or more systems for seizure expression, a sentiment shared by others (35,40).

Absence seizures

Absence seizures may be the least common seizure type of frontal lobe origin. Seizures are characterized by speech and behavioral arrest, staring, reduced to complete loss of consciousness, (sometimes with minor head and eye turning), and simple automatisms. There do not appear to be a preceding aura. Absences can be as short as 10 s, typical of absence seizures in the idiopathic generalized epilepsies, but may continue for 30 s or more and may have a longer postictal period before complete recovery. Seizures may progress further into generalized convulsions, often with complex or asymmetric motor features. Frontal absences have been described with ictal onset sites in the medial frontal gyrus (28), the anterior cingulate gyrus (24), and orbitofrontal cortex (40,41). Frontal absences have not been seen in patients with seizures from the SMA, and seem to originate from the
more anterior half of the mesial frontal cortex. One would hypothesize the areas maximally involved in the ictal discharge to have dense callosal connections, or projections to the thalamus, to account for the abrupt alteration of awareness and bilateral ictal EEG findings.

**Hypermotor seizures**

It must be admitted there is as yet no uniform acceptance of this term proposed by the Cleveland Clinic group. Complex motor seizures would also be appropriate, except that the term as used originally by Bancaud and colleagues referred to secondarily generalized seizures preceded by head and eye deviation, and unilateral posturing of the limbs (28). This seizure type is above all characterized by motor agitation charged with an emotional quality. A variable number of patients experience an aura at onset. The range of symptoms is very wide: viscerosensory symptoms such as chest, abdominal, or throat sensations, breathlessness, and palpitations; olfactory sensations probably via early seizure spread from orbitofrontal cortex to the entorhinal cortex of the temporal lobe (33), ill-localized somatosensory feelings of tingling, numbness, tightness, and heat; nonspecific lightheaded and cephalic sensations; experiential visual illusions and hallucinations; and emotional feelings including fear. Motor signs consist of early, complex large-amplitude movements that have been described variously as repetitive, stereotyped, perseverative, sexual (pelvic thrusting), bimanual-bipedal (thrashing), often bizarre and charged with an emotional, aggressive, or distressing quality. The behaviors are often accompanied by forced laughter, crying, whining, and vocalizations or verbalizations, which can sometimes be obscene. Urinary incontinence may occur. Consciousness is variably impaired, usually in relation to the intensity and duration of the seizure. Although many seizures are relatively brief (10–20 s), progression to a secondary convulsion is possible. Many patients have nocturnal seizures, sometimes exclusively. Hypermotor seizures are described to originate from the mesial frontal gyrus (26,42), the anterior cingulate cortex (1,28), and orbitofrontal and frontal polar regions (26,30,31,41,43,44). Studies of intracranial ictal EEG during frontal lobe seizures with bimanual–bipedal automatisms showed that lateral and mediofrontal structures were the most frequently involved, with spread to temporal structures only in a minority (45). When bimanual–bipedal automatisms occur during complex partial seizures of temporal lobe origin they were frequently associated with spread of the ictal discharge to orbitofrontal and lateral frontal regions.

**Postural tonic seizures**

These seizures typically arise from the posterior half of the medial frontal gyrus, corresponding to the SMA when functionally defined by electrical stimulation stud-

ies, but the epileptogenic zone can also involve or extend to the adjacent paracentral lobule, the cingulate gyrus, and the first frontal convolution dorsally (14,27,30,31,33,46–49). An aura is present in about half of the patients, usually somatosensory in nature, although rarely is it localized as in seizures from the parietal lobe. A whole body segment or more is involved in the aura, unilaterally or bilaterally. Sensations other than tingling or numbness are also described, such as tightness, “floating away,” or a sensation of movement. When lateralized, the somatosensory aura is contralateral to the hemisphere of seizure onset. The initial motor sign is usually that of bilateral but asymmetric tonic posturing of the extremities or if initially unilateral, the changes rapidly become bilateral. There may be an associated facial grimace or, as more appropriately described by Ajmone Marsan and Ralston (25), bilateral facial contraction producing a wide-eyed grin. The arms elevate and abduct but do not clear the head in every case. When they do, and one flexes while the other extends, one observes the classic fencing posture. The legs are involved and assume postures of flexion or extension. Vocalization occurs in about a third of cases, with a forced repetitive or affective quality. Truncal, pelvic, and bidel movements develop after the initial tonic phase in about a quarter of instances. Seizures often terminate at this stage, and hence seizures are often relatively short, in the range of 20–30 s. Focal clonic activity, if seen, develops later, usually in the course of secondary generalization, and can provide a reliable lateralizing sign. The same applies to head version, if it occurs at all. Manual automatisms are infrequent, fragmentary, and late in occurrence. Awareness and memory are retained in very brief seizures and become progressively impaired as the seizure intensifies. Nocturnal predominance of the seizures is again common.

**DIAGNOSTIC CONSIDERATIONS**

**Scalp EEG**

Findings are somewhat variable reflecting the large anatomic territory and the medial interhemispheric location of electrical generators. The medial frontal cortex is well recognized as a site for the generation of “secondary bilateral synchrony” (50). The reverse does not hold true, because bilateral discharges can arise not only from frontal parasagittal sites but also from medial parietal and temporal locations. It must be remembered that secondary bilateral synchrony is a hypothetical mechanism and that the term encompasses a variety of EEG phenomena (50). Interictal sharp waves from medial interhemispheric or high parasagittal generators are often not bilateral generalized discharges but are much more likely to represent midline discharges (Fig. 3). Transverse mon-
FIG. 3. Midline interictal sharp waves with Cz maximum in a patient with supplementary motor area epilepsy (patient 9, Table 1).

Epileptogenic zones at the frontal pole involving medial or orbitofrontal surfaces may exhibit localized or bilaterally symmetric or asymmetric frontal interictal sharp waves (30,41,44,51). Sometimes only slow waves are present. Detection may be aided by the placement of additional electrodes according to the 10–10 system or at supraorbital and infraorbital sites (44,52). Nasoethmoidal electrodes have also had some success in localizing discharges from the orbitofrontal cortex (53,54), but suffer from the disadvantages of requiring a special ENT procedure and of the lack of tolerability for long-term monitoring. However, the orbitofrontal cortex, anterior medial frontal gyrus, and cingulate gyrus are epileptogenic zones notorious for falsely localized interictal discharges, commonly over one or both temporal regions (26,31,41). Ictal scalp EEG recordings of seizures arising from these regions appear to be highly variable, and are often nonlocalizing.

The scalp EEG findings of epileptic foci in the intermediate portion of the mediofrontal gyrus may exhibit features of the type seen in SMA epilepsy or of those seen in orbitofrontal epilepsy. A clear picture is lacking. One category of seizures and its EEG characteristics deserves separate mention. It is sometimes seen in patients who appear to have frontal absence seizures. The ictal and interictal EEGs in some patients are striking for regular, rhythmic 2- to 3-Hz, generalized spike-and-wave, or multiple spike-and-wave complexes, maximal over the frontal regions, symmetrically or with voltage

tages and referential mapping of the potential field, including midline electrodes, usually make this clear. A parasagittal to midline potential localization is quite typical for patients with SMA epilepsy (27,49) and is seen in a majority of patients. NREM sleep often activates these discharges. Midline rhythmic slow waves, more commonly in the $\theta$ than in the $\delta$ range, are also not uncommon. Ictal EEG recordings in SMA epilepsy are often obscured by muscle artifact. However, a burst of vertex maximal sharp waves, or diffuse EEG attenuation can often be seen at onset before EMG artifacts make interpretation impossible (49). In longer seizures, rhythmic ictal activity may be glimpsed. Postictal depression and EEG slowing are functions of seizure intensity, clearly evident after secondarily generalized convulsions, but may be entirely absent after brief postural tonic seizures in SMA epilepsy. Both interictal and ictal EEG findings often make lateralization difficult if not impossible. Sometimes the voltage potential field is clearly asymmetric. The side of higher voltage more commonly than not is on the side of the epileptogenic zone, but the reverse has been seen. The scalp topographic field is probably influenced by the degree to which the dorsal convexity of the first frontal convolution is recruited in electrical generation. When it is recruited, voltage maximum is on the side of the generator. A deeper dipole generator in the medial interhemispheric surface, on the other hand, may "paradoxically" project the voltage field to the contralateral hemisphere.
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Predominance to one side (Fig. 4). Clues to secondary bilateral synchrony are sometimes found in independent or leading spikes, persistent amplitude asymmetry, or localized slow waves. These frontal absences have been shown to arise from the medial frontal region and from the cingulate gyrus (24,31,55). Techniques for the analysis for small time differences (56,57) may help to reveal a leading generator when applied to the scalp EEG. Other patients with frontal absence seizures may have more localized ictal EEG findings or no scalp EEG changes.

Intracranial EEG

Intracranial EEG is frequently called for in the presurgical evaluation of mesial frontal epilepsy except when a discrete structural abnormality is present that is entirely consistent with other data. Intracranial EEG is used to localize the epileptogenic zone among a number of possibilities, to lateralize the site of seizure onset even when approximate lobar location is known, and to integrate functional and EEG information to guide the plan of resection. Depth and subdural grid and strip electrodes each have their advantages and disadvantages, and their appropriate selection should be made with the particular situation and questions in mind for the individual case (49). For exploration of the medial frontal region, stereotactically implanted depth electrodes provide the greatest anatomic accuracy but also have the highest risk for intracerebral hemorrhage. By contrast, subdural strips are associated with low risk, but it can be difficult to ensure they are placed where they were intended to go. Subdural grids are most helpful when detailed functional and EEG information are needed for resections anticipated to be close to essential cortical areas.

A few points on the ictal EEG, as recorded by intracranial electrodes, will be mentioned. At onset, the ictal discharge frequency is often extremely fast (20–100 Hz) and of low amplitude (58,59). It can be mistaken for noise and artifact from cable movement and from the environment. An injudicious use of high-frequency filters will obliterate this signature. Ictal propagation to contralateral homologous structures (24,60) and to the dorsal convexity of the superior frontal gyrus is rapid (61). When symmetric depth or subdural electrodes have been placed, onsets can appear disconcertingly bilateral and simultaneous (10,24,60). High temporal resolution analysis for small time differences can help to reveal a leading site but is possible only with fast analogue-to-digital sampling well beyond the conventional 200-Hz sampling rate of most commercial systems. Frontal absences characterized by generalized spike-and-wave complexes on the scalp EEG unfortunately tend to appear identical when explored by intracranial electrodes. In these cases, an interictal “hot spot” may provide the only clue to the location of the epileptogenic zone.

FIG. 4. Ictal scalp EEG showing bilateral multiple spike-and-wave complexes of a frontal absence seizure in a patient with an anterior cingulate lesion (patient 11, Table 1).
Brain imaging

MRI can now reliably detect all tumors and AVMs and an increasing proportion of cortical dysgenetic lesions (Fig. 5). With the continuing improvements in MR imaging, it is difficult to estimate the sensitivity rate in lesion detection from case series just a few years old. Series from surgical centers are likely to be biased in favor of structural lesions because their presence helps in the surgical selection process. Recent MRI improvements include extremely high-resolution, 1-mm thickness contiguous slices, whole-brain SPGR acquisition, and FLAIR (fluid attenuated inversion recovery) sequences (62). Surface rendering to study gyral patterns can detect subtle areas of cortical dysgenesis (15), although this technique has been mainly applied to study of the cortical convexity rather than the fissures.

Earlier PET studies had occasionally found interictal glucose hypometabolism in patients with suspected frontal lobe epilepsy. More recent studies reported improved sensitivity of detection by quantitative techniques of analysis using regional templates normalized to controls (63–65). Quantitative studies were able to demonstrate localized interictal hypometabolism of 10 to 25% in various subregions. There have also been reports of reduced benzodiazepine receptor binding on flumazenil-labeled PET images of patients with frontal lobe epilepsy (66).

Ictal or immediate postictal SPECT imaging has been successful in several reports of patients with orbitofrontal, medial frontal, or SMA epilepsy (30,67). The difficulty in timely injection of the radioisotopic ligand in seizures that are often abrupt in onset and short in duration must be considerable. Not all centers have been able to replicate such a high rate of success.

The role of MR spectroscopy in frontal lobe epilepsy remains to be defined. In one report of eight patients with frontal lobe epilepsy (68), phosphorous MRS revealed interictal alkalosis in the epileptogenic lobe in all patients, and decreased phosphomonoester levels in 7.

OUTCOMES AND OPERATIVE TREATMENT

Given the relatively small number of patients with confirmed mesialfrontal epilepsy and that the confirmed cases were almost all selected for surgical treatment, it is
difficult to make broad generalizations on the course of condition. Etiologic factors are probably more important than the electroclinical localization in determining long-term outcome. Just as familial temporal lobe epilepsy (69,70) may present a relatively "benign" picture compared with that of mesial temporal sclerosis or temporal lobe lesions, so it appears that autosomal dominant nocturnal frontal lobe epilepsy may also show a more favorable course (18–20). There appears to be considerable variability in severity, but at least a third of patients achieved satisfactory control with carbamazepine (19). The clinical, EEG, PET and SPECT features of autosomal nocturnal frontal lobe epilepsy strongly suggest a mesial-frontal origin, either from the SMA or from more anterior medial frontal regions. Only intracranial EEG localization has yet to be attained.

A number of reports highlighted the associated psychopathology in frontal lobe epilepsy. Of 100 patients who underwent a frontal resection at the Hôpital St. Anne (11), 38% had problems of personality and behavior, with 10% rated as severe. In 36 patients with cingulate epilepsy who achieved a good surgical result, psychopathology was noted in 72%, with 55% rated as being in an “almost permanent major psychotic” state (24). Bursts of aggression, hostility, and agitation were notable. Other psychopathic abnormalities associated with cingulate epilepsy include obsessive–compulsive behaviors and sexual preoccupation (1,71). Many patients with hypermotor seizures or postural tonic seizures of medial frontal onset, have been misdiagnosed as having pseudoseizures (26,72). Eight of Williamson’s 10 patients were believed to be hysterical before epilepsy was diagnosed. Unlike the patients with cingulate epilepsy, those with SMA epilepsy do not appear to have a high rate of psychopathology.

Pharmacologic treatment follows the same principles as for other localization-related epilepsies. There is nothing in accumulated experience to suggest that frontal lobe epilepsies or the different seizure types of mesial frontal origin show a selective response to one or more AEDs.

Except in patients with a well-defined discrete structural lesion distant from the rolandic cortex, intracranial EEG investigation is a necessary prelude to the surgical treatment of mesial frontal epilepsy. Localization of essential functions is a critical part of the surgical planning process. Frontal corticectomies vary greatly in size and location and may be combined with partial section of the corpus callosum, undercutting of subcortical fiber tracts, and multiple subpial transection. The overall seizure outcomes after medial frontal resections are probably comparable to those after extratemporal neocortical resections as a whole. In the large series of 283 patients with nontumoral frontal lobe epilepsy who underwent surgery at the Montreal Neurological Institute, 36% became seizure-free or had only rare attacks (73). In 89 patients with some of the features of cingulate epilepsy and who underwent a frontal resection, 39 (44%) obtained a successful result with less than one seizure a year (24). Failures were most obvious in the 21 patients who only had excision of the convexity of the frontal lobe with only one obtaining a good result. Of another 31 patients at the Hôpital St. Anne (11) who had medial frontal corticectomies, the greatest improvement occurred in the group that had a posterior resection (80%), with the least success after mid-frontal (18%), and intermediate results after anterior frontal resections (50%).

At the Oregon Comprehensive Epilepsy Program, 32 patients underwent a frontal resective procedure (31 operated locally, with one patient operated elsewhere after presurgical evaluation) between 1982 and 1997. Eleven of the resections were primarily mesial frontal. Localization of a mesial frontal epileptogenic zone was obtained by subdural strips or grids or both in seven patients and was inferred from an imaged lesion in the other four. Altogether, seven patients had an imaged abnormality: three tumors, one each with cortical dysgenesis, AVM, scar from cerebral abscess, and lesion of indeterminate pathology. The resection was predominantly anterior (anterior half of the medial frontal gyrus, with or without removal of cingulate or orbitofrontal cortex) in eight patients (Fig. 5), and predominantly posterior (posterior half of the medial frontal and sometimes cingulate gyri), including the SMA, in two (Fig. 6). The adjacent first frontal convolution was usually also removed in the process. One patient had a cingulate lesionectomy. Six of the 11 patients (55%) obtained a good outcome, with five patients entirely seizure-free at 1-year follow-up.

FIG. 6. Postoperative MRI demonstrating resection of the right supplementary motor area with seizure-free outcome (patient 9, Table 1).
other patient only had nondisabling focal motor seizures postoperatively (Table 1).

There are several more series of patients with surgically treated mesial frontal epilepsy. All five patients in Williamson’s 1985 report who underwent a frontal resection for hypermotor seizures arising from mesial frontal or orbitofrontal regions became seizure-free or had only rare breakthrough seizures. Half of a group of eight patients who underwent limited resection of the mesial part of one frontal lobe became seizure free or almost seizure-free (34). This is mirrored by another 12 patients who underwent mesial frontal resections, half of whom were seizure-free or had only rare seizures (74). In the Cleveland Clinic series (60) of 20 patients who underwent corticectomies for SMA epilepsy guided by the results of subdural grid investigation, 10 (50%) were seizure-free (four) or had rare seizures (three), or had only residual nondisabling simple partial seizures (three). Four of eight patients from the Yale series who underwent surgery for SMA epilepsy became seizure-free (75). All five patients reported by Mihara et al. (76) were either seizure-free or had only rare seizures. Taking the combined experience of these more recent reports, it can be seen that some 58% of patients operated on for mesial frontal epilepsy have become seizure-free or almost seizure-free (Table 2).

Because the SMA is adjacent to the primary motor areas for the lower extremity and because the epileptogenic zone can extend to the rolandic cortex on the convexity, incomplete resection of the epileptogenic cortex often anticipates a less than perfect outcome. In addition to the completeness of resection, other factors reported to influence seizure outcome after operation on the frontal lobe (11) include the presence of a localized lesion which improved surgical success, although too-extensive cerebral damage from head trauma diminished the results. Frontal resections that included subcortical fibers of the corona radiata were felt to have a better seizure outcome than when these same fiber tracts were preserved (11). Some patients who had poorly lateralized EEG findings and who were nevertheless suspected to have medial frontal epilepsy have been treated with corpus callosotomy, but the results have been quite variable and difficult to interpret (39).

Surgical complications and deficits have thus far not proved to be a limiting factor for operations on the mediofrontal region except at its posterior limit, where removal of primary motor areas would lead to unacceptable loss of function. Detailed consideration must be given to vascular anatomy, because interruption of venous drainage after removal of the superior frontal gyrus can lead to edema and hemorrhagic complications (77). Removal of the medial frontal gyrus anterior to the SMA appear to produce no complications. SMA resection is now well recognized to often produce a temporary state of profound contralateral weakness with mutism (49,60, 78,79). The weakness has been described to be accompanied by hypotonia, normal tone, or hypertonia, with normal to increased reflexes. There is also a superimposed akinesia so that movements are diminished bilat-

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GTCS, generalized tonic-clonic seizure, outcome classes I to IV according to Engel classification; ant, anterior; lat, lateral; front, frontal.
TABLE 2. Surgical outcome in mesial frontal epilepsy

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<th>Study</th>
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<td>Mihara et al.</td>
<td>1996</td>
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<td>Smith and King</td>
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<td>12</td>
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<tr>
<td>Spencer et al.</td>
<td>1996</td>
<td>8</td>
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<td>OCEP</td>
<td>1997</td>
<td>11</td>
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<tr>
<td>Total</td>
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<td>69</td>
<td>40 (58%)</td>
</tr>
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52. Quesney LF. Seizures of frontal lobe origin. In: Pedley TA, Mel-


