

## Clinical and Radiologic Correlates of Frontal Intermittent Rhythmic Delta Activity

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To assess the clinical and radiologic correlates of frontal intermittent rhythmic  $\delta$  activity (FIRDA), the authors reviewed the hospital charts of patients whose EEGs depicted this EEG finding, and recorded their past medical and neurologic history, the reason for hospital admission, and their neurologic status both on admission and during EEG recordings. Laboratory results on admission and concomitant to the EEG recording, computed tomography, or MRI findings during hospital admission were also reviewed. Sixty-eight patients were assessed. The gender ratio was 1:1; mean age was 56 years. Chronic disease occurred in 78% of patients, including hypertension (34%), diabetes (32%), and renal failure (18%). On admission, renal failure ( $n = 34$ ) and hyperglycemia ( $n = 22$ ) were most prominent. The majority of patients had at least one abnormal laboratory result. Thirty-eight of 51 patients in whom the level of consciousness was stated during EEG were described as awake. More than half of 58 patients whose EEG background activity was stipulated demonstrated diffuse slowing, mostly in the  $\theta$  range. MRI was abnormal in 15 of 17 patients. Intrahemispheric lesions, particularly ischemic and hemorrhagic, were most common ( $n = 10$ ), followed by basal ganglia lacunae ( $n = 4$ ). Computed tomography was abnormal in 29 of 44 patients. Hemispheric pathology, diffuse or localized, occurred in 22 patients. Frontal intermittent rhythmic  $\delta$  activity is associated with mild to moderate encephalopathy and is detected principally in awake patients. Most patients in this series had chronic systemic illness. Old ischemic structural brain lesions may predispose some patients to develop FIRDA during acute metabolic derangement, such as uremia and hyperglycemia. Frontal intermittent rhythmic  $\delta$  activity was not associated with EEG epileptiform activity. Deep midline lesions, posterior fossa tumors, and hydrocephalus were not detected in this series of patients with FIRDA. **Key Words:** FIRDA—Clinical—Radiologic—Correlates.

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Frontal intermittent rhythmic  $\delta$  activity (FIRDA) is a transient EEG finding in adults. Originally described by Cobb (1945), it was attributed initially to deep midline lesions (Faure et al., 1951) and posterior fossa tumors (Daly et al., 1953). However, it has also been reported in associ-

ation with third ventricle and pituitary tumors, subcortical lesions, hydrocephalus, cerebral edema, increased intracranial pressure, and acute confusional migraine (Hooshmand, 1983; Kameda et al., 1995; Pietrini et al., 1987). Metabolic derangement was present in 22% of patients, involving uremia and liver failure (Fariello et al., 1982). The pathophysiologic importance of FIRDA is unknown.

The aim of this study was to determine whether certain clinical, laboratory, and radiologic parameters

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are associated with the occurrence of FIRDA in acute situations.

## METHODS

EEGs performed between January 1992 and January 1998 were analyzed retrospectively for the keyword FIRDA or frontal intermittent  $\delta$  activity from our computerized database at the neurophysiology laboratory of the Medical College of Virginia. Demographic data included age, gender, and race. Past medical and neurologic history, clinical symptoms and signs, chronic medications, antiepileptic drugs, and neurologic findings were recorded. Indications for the current EEG, medications taken by the patient, EEG background activity, presence or absence of epileptiform discharges, and consciousness during the recording were also analyzed.

Laboratory data included full blood count; serum electrolytes; glucose, kidney, and liver function tests; calcium, magnesium, phosphorus, ammonia, creatine kinase, and blood gas analysis; cerebrospinal fluid results, and opening pressure. Blood, cerebrospinal fluid, urine, and other culture results; urine toxic screen for drugs of abuse and unknown drugs; and urinalyses were also recorded. Neuroradiologic studies included head computed tomography (CT) and MRI, and cerebral angiography.

## RESULTS

Approximately 22,000 EEG recordings were performed during the specified period. Frontal intermittent rhythmic  $\delta$  activity was detected in 147 cases. Sixty-eight medical records were available for analysis. Three patients had FIRDA on two different occasions.

The male-to-female ratio was equal, with a mean age of 56 years (range, 1 to 83 years). All but one patient were older than 20 years of age. Forty-two patients (65%) were black, 22 (33.8%) were white, and one was Asian. Most patients (63%) were admitted for neurologic conditions (Table 1). Hypertension (34%), diabetes mellitus (32%), and renal failure (18%) constituted the most prevalent forms of chronic disease. Meningoencephalitis, previous subarachnoid hemorrhage, Parkinson's disease, and epilepsy were the most common previous neurologic insults. Information on previous neurologic history was not available for 45% of patients. Of the remaining patients, less than 20% had sustained previous neurologic injury.

Most patients (76%) were on chronic medications. Benzodiazepines (21%), insulin (19%), aspirin (16%), and ranitidine (15%) were most prevalent.

**TABLE 1.** Indications for hospital admission in patients with FIRDA

Reason for Admission	n	%
Seizure	16	23.5
Suspected stroke	12	17.6
Metabolic	10	14.7
Status epilepticus	7	10.3
Altered mental status	5	7.4
Not specified	4	5.9
Trauma	3	4.4

The reason for hospital admission is shown in Table 1. Although many conditions led to hospitalization, seizures, stroke, and metabolic derangement constituted the reason for admission in well over half the patients.

Indications for EEG included possible seizures in 44 of 68 patients, altered mental status in 9, not specified in 8 patients, and recent status epilepticus in 7. More than 55% were awake during the recording, 10.3% were confused, 9.7% were lethargic/comatose, and in 25% the state of consciousness was not specified. Among the 51 patients for whom it was noted, 74.5% were awake, 13.7% were confused, and 11.8% were lethargic or comatose. EEG background activity was mildly to moderately slow in most cases. Normal wakefulness (posterior  $\alpha$  rhythm) background occurred in 17%. Epileptiform discharges occurred in 9% of patients.

Table 2 depicts the neurologic findings in this series. Although some significant positive or negative neurologic findings were detected in more than two-thirds of patients, none of these findings was particularly prominent. Thirty-two percent of patients were neurologically normal on admission.

Renal function impairment was present in 34 patients (50%), hyperglycemia alone in 22, and a combination of both in 25 patients. Abnormal liver enzymes were present in 19 patients. However, in the majority of these patients only one abnormal value occurred. Metabolic

**TABLE 2.** Neurologic findings on admission in patients with FIRDA

Neurologic finding	n	%
Normal examination	22	32.4
Left hemiparesis	9	13.2
Dementia	8	11.8
Lethargy	6	8.8
Confusion	5	7.4
Right hemiparesis	4	5.9
Parkinsonism	3	4.4
Coma	3	4.4

acidosis (low serum bicarbonate) was detected in five patients. Bacterial infections, thyroid dysfunction, electrolyte imbalance, and hyperammonemia were rare or were not found.

Head MRI was abnormal in 15 of 17 patients. Intrahemispheric lesions, particularly old ischemic and hemorrhagic ones, were most common ( $n = 10$ ), followed by basal ganglia lacunae ( $n = 4$ ). Computed tomography was abnormal in 29 of 44 studies. Hemispheric pathology occurred in 22 patients: It was diffuse in 41%, frontal in 23%, and occipital in 14%. Periventricular white matter disease ( $n = 8$ ) and diencephalic lesions ( $n = 6$ ) were also common. Most lesions on MRI and CT were ischemic in nature. Neuroimaging studies were performed in eight of nine patients whose EEG depicted normal  $\alpha$  rhythm. Three had normal studies. Subacute or chronic subcortical ischemic lesions were present in four patients, and mild ventricular dilatation in one. There were no cases of brain tumors, hydrocephalus, or midline lesions.

## DISCUSSION

Following the initial description in 1945 (Cobb, 1945), Van der Drift and Magnus (1959) coined the term *frontal intermittent rhythmic  $\delta$  activity* (FIRDA) in reference to a rhythmic slow-wave discharge localized in the frontal regions with a frequency of 1.5 to 4.0 cycles per second. This pattern, occurring in the waking adult EEG was attributed first to epithalamic tumors (Hooshmand, 1983) and later to deep midline and posterior fossa pathology (Bagchi et al., 1961; Daly et al., 1953). For several decades this notion was commonly accepted among neurologists and electroencephalographers (Faure et al., 1951). Subsequently it was shown that deep midline lesions were present only in a minority of patients with FIRDA (Fariello et al., 1982; Schaul et al., 1981; Van der Drift and Magnus, 1959). However, Fariello et al. (1982), analyzing 80 patients with FIRDA including 62 with concomitant CT scans, found brain structural abnormalities in more than 77% of patients. No diencephalic or infratentorial lesions were detected. Hemispheric brain tumors and ischemic brain injury were most prominent. Patients with no demonstrable brain lesions were more likely to have metabolic derangement, alteration of consciousness, and an abnormal EEG background (Fariello et al., 1982). The origin of this rhythm is still unclear. Previous speculation suggested that FIRDA represents a projected rhythm from subcortical, deep midline structures. However, although the origin of this rhythm is still unclear, recent research suggests that FIRDA reflects a pathologic type of hyperactivity typical

of gray matter disease (Stam and Pritchard, 1999). Conversely, polymorphic, irregular, and localized  $\delta$  activity occurs mostly in focal white matter lesions or, less commonly, in thalamic lesions (Gloor et al., 1977).

In a previous study of the MRI correlates of FIRDA in 27 patients, diffuse cerebral structural lesions, namely periventricular white matter disease and cortical atrophy of varying severity, were the most prevalent pathologic findings. Often, subacute or old focal ischemic abnormalities such as basal ganglia lacunae, thalamic lacunae, and cerebellar infarcts were also present. Acute hemispheric stroke, deep midline lesions, and posterior fossa tumors were conspicuously absent in this series (Waternberg and Towne, 1997). Previously, two studies assessed the CT correlates of FIRDA. In one series, in which shifting of midline structures was evaluated specifically, there was no evidence of mass effect in 23 of 26 patients (Scollo-Lavizzari and Matthis, 1981). Fariello et al. (1982) studied 80 patients with FIRDA and detected focal structural lesions in 44%, diffuse structural changes in 34%, and no abnormalities in 22%.

In the current series, ischemic brain disease, both diffuse and localized (previous strokes), were the most common radiologic findings. Both MRI studies ( $n = 17$ ) and CT scans ( $n = 29$ ) were obtained during the same hospitalization. At our institution, essentially all patients who become encephalopathic or experience seizures receive an EEG. Most patients with brain tumors and an abnormal neurologic status or seizures would have been assessed by this diagnostic means. Therefore, we feel that the absence of brain tumors, both located in the posterior fossa and midline in patients with FIRDA, represents a true negative correlation.

A comparison between 42 awake EEG records depicting FIRDA and 42 age-matched control subjects showed that FIRDA patients had a significantly higher incidence of diffuse encephalopathy than the control group. Deep midline lesions were not detected. Increased intracranial pressure was present in only 1 of the 62 FIRDA patients (Schaul et al., 1981). More recently a normal EEG background was shown to be significantly more common in patients with focal brain lesions than in those with diffuse lesions, metabolic derangement, or postictal states (Neufeld et al., 1999). Indeed, FIRDA seems more likely to occur in acutely ill patients with altered consciousness, and disappears within days to weeks (Hooshmand, 1983).

In our series, FIRDA occurred more commonly in elderly patients with chronic hypertension, diabetes mellitus, or renal disease. Because there was no control group, the true importance of previous chronic illness in this population cannot be ascertained. However, only a

minority of patients had no previous notable medical history. The association of FIRDA and metabolic derangement has received relatively little attention in the medical literature. This could in part be the result of the fact that rhythmic  $\delta$  activity occurring in the setting of a slow EEG background, as in the case of metabolic encephalopathy, may not be labeled as FIRDA. On the other hand, FIRDA may be more likely to be described on EEG recordings of awake individuals with normal background activity. Among patients with chronic renal failure receiving chronic hemodialysis, the occurrence of FIRDA and frontocentral spike-and-wave discharges correlated with the development of dialytic encephalopathy. Both findings were uncommon in chronic renal failure patients who did not develop dialytic encephalopathy (Chokroverty and Gandhi, 1982). Other chronic metabolic conditions have not been reported in association with FIRDA. In our series, renal failure was present in half of cases. However, most of these cases involved acute renal failure, and only 12% had end-stage renal disease. In fact, we found abnormal serum glucose levels, alone or in combination with impaired renal functions, to be most prominent in patients with FIRDA.

Of 51 patients for whom information was available regarding their level of consciousness, 75% were awake when FIRDA occurred. However, only 17% had a normal posterior  $\alpha$  rhythm. This apparent discrepancy between the clinical state of the patient and the lack of electrographic evidence of wakefulness possibly indicates a mild degree of encephalopathy that was not obvious to the EEG technologist. Although FIRDA is more likely to occur during periods of altered consciousness in the elderly (Hooshmand, 1983; Scollo-Lavizzari and Matthis, 1981; Wasler and Isler, 1982), some series on younger patients suggest that the occurrence of this rhythm during wakefulness may be common in this age group (Kubota and Ohnishi, 1997; Mutoh et al., 1992).

In our series, acute seizures or the need to rule out interictal epileptiform activity were the most common indications to obtain an EEG. Sharp waves and spikes were detected in only 9% of cases. Moreover, among the seven patients admitted for convulsive or nonconvulsive status epilepticus, only one case depicted epileptiform activity on the EEG tracing. EEGs were performed on admission in all cases of status epilepticus and on those patients who remained lethargic or comatose after the event. Thus, essentially all cases of nonconvulsive status epilepticus were detected (DeLorenzo et al., 1998). All postictal EEG recordings depicting FIRDA were performed during a seizure-free period, usually 24 to 48 hours after the clinical event. Frontal intermittent rhythmic  $\delta$  activity was absent in EEGs obtained during

seizures or immediately after ictal episodes or status epilepticus.

There is evidence that FIRDA may be associated with epileptiform activity in some cases. Rhythmic 3-Hz slow-wave bursts occur sometimes in the frontal areas of epileptic patients, particularly in absence epilepsy (Anders and Ingrid, 1991). A recent study evaluated the clinical correlations of FIRDA among epileptic patients (Kubota and Ohnishi, 1997). Two groups of patients were identified, according to the frequency of the frontal rhythmic  $\delta$  discharges. Individuals with FIRDA bursts of 1.5 to 2.5 Hz were older and most had partial epilepsy. In contrast, patients with 3-Hz FIRDA were younger and had idiopathic generalized epilepsy. However, FIRDA was uncommon among epileptic patients, occurring in less than 2% of patients.

Interictal epileptiform activity was relatively common in our series, being detected in six patients. This probably reflects the fact that most EEGs were performed after a seizure. However, the epileptiform discharges were either focal or located outside the frontal leads, and none intermixed with FIRDA. No cases of idiopathic generalized epilepsy were detected. Presumably, frontal  $\delta$  activity in tracings depicting generalized spike-and-wave activity may not have been classified as FIRDA by the electroencephalographer.

The neurologic findings of our patient population (see Table 2) were varied and not specific. Approximately one-third had no neurologic findings. A similar proportion of patients presented with dementia or varying degrees of altered mental status, including three patients with coma. Other than altered consciousness, FIRDA has not been associated with any specific neurologic findings. It is likely, that in our series, these findings reflect the underlying brain pathology, and bear no relation with the presence or absence of FIRDA.

Although three-quarters of the patients were receiving chronic medications, there was no association between a specific drug type and FIRDA. Only one-third were on chronic antiepileptic drug treatment. Indeed, there are no reports in the literature of a possible association between FIRDA and chronic medications. The appearance of FIRDA does not appear to be caused or influenced by chronic oral medications.

This study is limited by the lack of information on follow-up EEGs in our patients and by the fact that concurrent clinical information was available for only 55% of patients with FIRDA. However, our findings suggest that FIRDA occurs in patients with diffuse structural brain injury during mild to moderate metabolic impairment. Although in many cases FIRDA is detected after seizures, it does not appear to be epileptic in nature,

but rather associated with transient cerebral dysfunction, either postictal or metabolic.

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