INTRODUCTION: EEG IN DEMENTIA AND HEREDITARY ENCEPHALOPATHIES

EEG has been employed clinically for some time as a measure of brain function in the hope of determining and differentiating certain functional conditions of the brain. It is used in patients who suffer from cognitive dysfunction, either a general decline of overall brain function or a localized or lateralized deficit. This article addresses primarily the clinical use of EEG in evaluation of dementias and encephalopathies. In addition, aspects of digital EEG and other newer developments are discussed briefly at the end of the article.

Definition of dementia

Criteria from Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) should be used in the diagnosis of dementia. Clinical dementia is a fairly broad-based decline of brain function; most definitions center on the patient’s intellectual decline and memory dysfunction. This is, however, a fairly simplistic approach; dementia is much more than these fundamental deficits. Some of the dementias have distinguishing features. The process that constitutes normal aging is still an ongoing debate. As our understanding and testing procedures develop, more people are being classified as suffering from some type of dementia.

In 1998, Widagdo et al performed a quantitative EEG (QEEG) study of age-related changes during cognitive tasks. This study revealed no conclusive differences between the young and the elderly. Cognitive decline, unlike normal aging, is associated with alterations in the temporospatial characteristics of EEG. The diagnosis of the initial stages of dementia is based mainly on neuropsychological testing and clinical suspicion. The EEG findings are nonspecific.

EEG findings in dementia

In early dementia, the resting alpha frequency declines. Most authors agree that the lower limit of normal alpha frequency is 8.5 cycles per second. Medications can slow the posterior dominant rhythm; therefore, medication effect should always be excluded. In assessing the frequency of the alpha rhythm, alerting maneuvers are essential in order to ensure that the patient is in the best awake state and not drowsy. Computerized methods, such as EEG spectral analysis, coherence, and complexity (ie, correlation dimension), have been demonstrated to correspond to cognitive function.

Stevens et al recorded EEGs during 2 resting conditions (eyes closed and eyes opened) and 2 tasks (mental arithmetic and a lexical decision). The goal of the study was to evaluate which temporal and spatial EEG descriptors change with cognitive decline and normal aging. The EEGs were analyzed by using EEG microstates. The primary findings were a significant increase in the number of ultrashort EEG microstates and a reduction in the average duration of EEG microstates in cognitively impaired and demented patients. Cognitive impairment was associated with a reduction or loss of EEG reactivity. In contrast, no alterations in temporal or spatial EEG descriptors were found in normal aging. Cognitive tasks did not add to the information already obtained during the resting states. The reduction in EEG microstate duration correlated with loss of cognitive function.

Therefore, temporospatial analysis of the EEG record is a useful indicator of cortical dysfunction in dementia and correlates with degree of cognitive impairment. Apparently, temporospatial analysis may be useful in distinguishing patients with dementia from those experiencing normal aging. These data are largely preliminary; whether they contribute additional information to the clinical data in evaluating dementia is unclear.

Definition of encephalopathy

Encephalopathy represents a brain state in which normal functioning of the brain is disturbed temporarily or permanently. Encephalopathy encompasses a number of conditions that lead to cognitive dysfunction. Some of these conditions are multifactorial and some have an established cause, such as hepatic or uremic encephalopathy. Because the EEG patterns in most dementias and encephalopathies demonstrate few specific features, they are discussed together. Some notable exceptions include Creutzfeldt-Jakob disease (CJD) and subacute sclerosing panencephalitis (SSPE); however, no specific patterns exist for most dementias and encephalopathies. Other conditions, such as hepatic and renal encephalopathies, carry distinguishing features; nevertheless, similar patterns may be seen in a fairly wide range of illnesses under certain conditions.
**EEG findings in encephalopathy**

In general, the most prominent feature of the EEG record in encephalopathies (if there is a change) is slowing of the normal background frequency. A gradual and progressive decline over the course of the disease may be noted if serial EEGs are performed. Disorganization of the record may develop gradually. Reactivity to photic or other type of external stimulation may be altered. If a QEEG is done, it may show a frequency shift or decreased interhemispheric coherence of background frequencies. Some conditions are associated with an increase in seizure frequency, and in such cases, epileptic activity may be recorded.

In a given context, the EEG can play a clinically useful role, especially since functional MRI, positron emission tomography (PET), and single-photon emission computed tomography (SPECT) are either still in an experimental stage or require special settings not widely available.

**Use of digital EEG data**

Although in the following sections digital EEG data are cited frequently, these data represent primarily digital analysis of clinical EEG recording. The referenced data are presumed to be based on an EEG recording that is read by a clinician; presently, it is recorded by using computerized technology for ease and also for availability for further analysis. A variety of mathematical transforms are available after the initial clinical interpretation—for example, coherence, Fourier transform, wavelets, and microstates (see Digital EEG). These allow for further comparisons with norms and control groups but should be interpreted in conjunction with the primary EEG reading.

### EEG FINDINGS IN DEMENTIA

**Alzheimer disease**

EEG is the only clinical diagnostic instrument directly reflecting cortical neuronal functioning. Although the EEG may be normal or minimally disturbed in a number of patients in the initial stages of Alzheimer disease (AD), an abnormal EEG usually is recorded later in the course. A large percentage of patients with moderately severe to severe AD exhibit abnormal EEGs.

In 1981, Stigsby reported diffuse increases of delta and theta frequencies, as well as decreases in the alpha and beta frequency ranges in AD. Frontal slowing was more prominent. The slowing was more prominent anterior to the sylvian fissure, while the blood flow was more decreased posterior to the sylvian fissure. These findings may be explained by the fact that the EEG reflects the functional decline of the anterior structures, while the flow decrease correlates more with the structural damage of the parietal lobe. The frontal slowing probably reflects the loss of functioning of the frontal cholinergic system.

Wada et al showed that EEG coherence provides a measure of functional correlation between 2 EEG signals. They examined intrahemispheric EEG coherence at rest and during photic stimulation in 10 patients with dementia of the Alzheimer type. In the resting EEG, patients with AD had significantly lower coherence than gender- and age-matched healthy control subjects in the alpha-1, alpha-2, and beta-1 frequency bands. EEG analysis during photic stimulation demonstrated that the patients had significantly lower coherence, irrespective of the stimulus frequency. The changes in coherence from the resting state to the stimulus condition showed significant group differences in the region of the brain primarily involved in visual functioning. The patients had significantly lower coherence of their EEG reactivity to photic stimulation at 5 and 15 Hz over the posterior head regions.

These findings suggest that patients with AD may have an impairment of interhemispheric functional connectivity in both nonstimulus and stimulus conditions. This suggests a failure of normal stimulation-related brain activation in AD. Jelic et al found a positive correlation between levels of tau protein in the cerebrospinal fluid (CSF) and EEG alpha/delta ratio. In a subgroup with high CSF tau levels, a strong relationship between EEG alpha/theta and alpha/delta power was found. No such correlation was found in healthy controls and mildly cognitively impaired individuals with elevated CSF tau levels.

Locatelli et al used EEG coherence to evaluate the functionality of cortical connections and to get information about the synchronization of the regional cortical activity. They studied EEG coherence in patients with suspected AD. Alpha coherence was decreased significantly in 6 patients. Significant delta coherence increase was found in a few patients between frontal and posterior regions. The group with AD demonstrated a significant decrease of alpha-band coherence in the tempo-parieto-occipital areas. This was expressed to a greater extent in patients with more severe cognitive impairment. They theorized that these abnormalities could reflect 2 different pathophysiological changes: (1) the alpha coherence decrease could be related to alterations in corticocortical connections, whereas (2) the delta coherence increase suggests lack of influence of subcortical cholinergic structures on cortical electrical activity.

Strik et al studied EEG microstates in AD. The microstates of the resting EEG of patients presenting with mild or moderately severe dementia of the Alzheimer type demonstrated a significant anteriorization of the microstate fields, and the duration of sustained microstates was reduced. These differences were more important than the diffuse slowing. The measurements of microstates may be useful in the early diagnosis of AD. Muller et al conducted a study comparing SPECT and QEEG. They concluded that QEEG may be as useful as SPECT brain scanning in staging the disease; however, the correlation with clinical status was weak.
Siennicki-Lantz et al studied the relation of cerebral white matter lesions to AD. Cerebral blood flow (CBF) in white matter correlated with systolic blood pressure and multichannel EEG in senile dementia of the Alzheimer type. The presence and functional significance of white matter lesions in the aging brain or in dementia and their relation to blood pressure is an unsettled issue. White matter lesions occur in both cerebrovascular disease and AD. Probably, the white matter lesions in hypertensive patients are not related to but simply are coexistent with the AD. Their influence on overall expression of the degree of dementia is unclear; intuitively, however, the lesions should be causing additional cognitive dysfunction.

They observed significantly lower CBF in the white matter (WMCBF) in patients with AD than in controls. This was more obvious in the posterior cerebral region (ie, parieto-temporo-occipital area). QEEG from the posterior cerebral regions correlated with WMCBF. Systolic blood pressure was significantly lower in the AD group and was correlated positively with WMCBF in the posterior and anterior brain regions. Epileptiform activity may occur more frequently in patients with AD than in the general population; clinical tonic-clonic seizures can occur. Bilateral synchronous periodic epileptiform discharges (BiPEDs), such as triphasic waves (TWs), may be recorded in AD, usually in the late stages (for more information on TWs, see Triphasic Waveforms). These findings are not specific for AD because they most often are observed in metabolic disorders, particularly hepatic encephalopathy and other degenerative diseases, such as CJD. While good correlation exists between severity of EEG abnormalities and cognitive impairment, epileptiform discharges or TWs are not predictive factors for seizures. EEG often can be useful in evaluating dementia in order to exclude a superimposed reversible metabolic etiology, and to confirm CJD when the dementia is rapidly progressive.

To investigate the relationship between QEEG band powers and CBF, Rodriguez et al studied 42 patients with suspected AD and 18 healthy controls who were elderly. They tried to differentiate patients with AD from the controls by QEEG and CBF measurements. Regional CBF and QEEG were correlated with one another, especially in the right hemisphere. Significant correlations were found between Mini Mental State Examination (MMSE) scores and relative power of the 2- to 6-Hz and the 6.5- to 12-Hz bands on either side and between MMSE scores and left regional CBF, while the correlation between MMSE scores and right regional CBF was less strong.

Employed together, QEEG and regional CBF sensitivity was 88% and specificity 89%, with a total accuracy of 88.3%. QEEG alone showed an accuracy of 77% in the whole group and of 69% in those with mild AD, and regional CBF alone an accuracy of 75% in the whole group and of 71% in those with mild AD. This study suggests that QEEG and regional CBF measurements used together are reasonably accurate in differentiating AD from healthy aging.

Lehtovirta et al studied the relation of apolipoprotein E (ApoE) to EEG changes. ApoE sigma-4 allele is a risk factor for late-onset AD and is proposed to have an impact on cholinergic function in AD. Because the cholinergic system has an important role in modulating EEG, an impairment of the cholinergic system may have a relation to the EEG slowing that is characteristic of AD progression. The QEEG of 31 patients with AD was recorded at the early stage of the disease and after a 3-year follow-up. Patients with AD were divided into several subgroups according to the ApoE sigma-4 allele (ie, 2 sigma-4, 1 sigma-4, and 0 sigma-4). These subgroups did not differ in clinical severity or duration of dementia. The AD patients carrying the sigma-4 allele had more pronounced slow-wave activity than AD patients without the sigma-4 allele, although the disease progression rate did not change. These differences in EEG may suggest differences in the degree of the cholinergic deficit in these subgroups.

The typical electrophysiological correlates of myoclonus in AD are similar to those of cortical reflex myoclonus, with a focal, contralateral negativity in the EEG preceding the myoclonic jerk. The electrophysiological correlate of polymyoclonus that can be seen in AD and other pathological states is a bifrontal negativity in the EEG that precedes the myoclonic jerk. This new type of electrophysiological correlate of myoclonus may reflect activity of a subcortical generator.

◆ Pick disease

Pick disease, which is a frontotemporal dementia, is much less common than AD. The age of onset is earlier than that of AD. The EEG is less abnormal than in AD, especially in the early stages. Posterior alpha rhythm is more preserved. Theta and delta are increased. Frequency analysis may demonstrate a difference at a time when simple visual reading may not pick up a clear abnormality. The major feature of Pick disease is a decline in judgment and insight with relative early preservation of memory. Because EEG correlates poorly with the clinical symptoms, impressive EEG changes are not observed in this condition. Blood flow measurements correlate with thinking processes; Ingvar demonstrated these changes in 1977. Stigosby demonstrated a decrease in anterior blood flow in patients with Pick disease. Because the anterior cholinergic system is relatively preserved in Pick disease, the EEG changes are not prominent frontally.

◆ Huntington chorea

Huntington chorea is a combination of a movement disorder and a dementia, which is dominated by cognitive impairment, psychotic features, and memory impairment. The EEG changes show gradual and progressive slowing over time. The amplitude also attenuates as the disease progresses. About 30% of the patients have very-low-voltage EEGs with amplitudes below 10 microvolts. Hyperventilation as a rule does not increase the background voltage as it usually does in healthy subjects. About 3% of the patients show epileptiform activity; they tend to be juvenile cases. The EEG has not been proven to be of any predictive value in identifying future affected family members. Genetic testing is far more useful.
**Progressive supranuclear palsy**

In progressive supranuclear palsy (PSP), usually the degree of dementia is not severe. The EEG may be normal initially but eventually shows increasing delta and theta activity. The delta may be rhythmic with frontal accentuation. Gross et al showed a decrease in background frequency down to 6-7/s and delta activity over the temporal regions. Sleep may show poor spindle development. Rapid eye movement (REM) sleep may be reduced or absent. These changes probably reflect the involvement of the locus ceruleus and the pontine raphe nuclei.

**Parkinson disease**

The EEG is frequently normal. In advanced cases, however, marked slowing is noted. Sleep may be markedly abnormal with frequent awakenings, prolonged sleep latency, reduced REM sleep, periodic leg movements, etc. Wszolek et al studied patients with rapidly progressive familial parkinsonism and dementia with pallidopontonigral degeneration (PPND). The patients had PPND linked to chromosome 17q21-22; 11 EEGs of 9 patients were studied. EEGs revealed normal findings early in the disease and diffuse slowing that became more prominent with disease progression. Electromyograms (EMGs) and nerve conduction studies (NCSs) showed no abnormalities. Visual evoked potentials (VEPs) and sensory evoked potentials (SEPs) were normal. The clinical neurophysiologic study findings were consistent with a cortical and subcortical degenerative process.

With clinical deterioration, progressive decline is seen in the mean parietal frequency and background rhythms. Theta and theta-delta mixture may be recorded bilaterally in the posterior head regions. After stereotactic surgery, focal theta or delta slowing may be observed.

**Binswanger disease**

Binswanger disease usually demonstrates slowing of background and a nonspecific pattern; however, Kuroda et al reported some other patterns. They described a 72-year-old patient with von Recklinghausen disease exhibiting akinetic mutism within 6 months of the onset of dementia. The EEG demonstrated periodic synchronous discharges (PSDs) suggesting CJD. The CT brain scan findings represented diffuse cerebral atrophy. Autopsy findings revealed diffuse subcortical white matter disease and marked arteriosclerotic changes of the subcortical arterioles. The cortex was relatively spared, and the pathologic diagnosis confirmed Binswanger disease. Binswanger disease, therefore, can present with PSD and should be included in the differential diagnosis of dementia. On the other hand, Dziaiek et al described a group of 15 patients with Binswanger subcortical atherosclerotic encephalopathy who showed different EEG appearance. The EEG records were pathological in most cases, with varying degrees of slow activity that was distributed symmetrically.

**Circulatory encephalopathy**

- **Atherosclerosis**

Plachinda et al studied the correlations of cognitive disorders and the EEGs of elderly patients with circulatory encephalopathy. They explored the possibilities of using EEG for evaluating intellectual-mnemonic disorders in elderly patients with cerebral atherosclerosis. Ninety-five patients (aged 60-74 years) with atherosclerotic encephalopathy but without stroke were included in the study. Statistical analysis of the data demonstrated a correlation between psychological test results and EEG readings and computerized EEG data. In cerebrovascular disease, focal slowing is far more frequent than in nonvascular dementia; therefore, EEG can be useful in distinguishing the 2 conditions.

- **Multi-infarct dementia**

No specific EEG pattern is associated with multi-infarct dementia. Some background slowing may be observed, especially in advanced disease. These changes are less prominent and do not show the progressive course observed in AD. Research is very scanty. Edman et al found a significant relationship between the increase in EEG slow-wave activity and increases in severity of the parietal brain syndrome. A somewhat lower significance was found for the relation between the increase in slow-wave activity and increases in the degree of dementia. These results suggest that the EEG deterioration mainly reflects the progressive and gradual decline of parietal brain function.

Iznak et al used QEEG to reveal the specific features of and study amplitude-frequency parameters in patients with mild dementia of different origins compared to healthy elderly individuals. They found that alpha rhythm was suppressed in AD and vascular dementia and that alpha rhythm was slower and theta activity higher in AD. Patients with AD were characterized by desynchronized EEG.

- **Transient global amnesia**

A variety of records have been reported from normal to even epileptiform potentials in transient global amnesia (TGA). Nonepileptiform activity, such as bitemporal delta or bioccipital theta, has been reported. Kushner described patients with normal activity, one with occasional epileptic activity, and one with asymmetric alpha depression, while 2 patients had intermittent rhythmic slowing. TGA caused by a seizure is uncommon, and is believed to be caused by a vascular etiology or spreading depression. Patients with Korsakoff syndrome often have abnormal EEGs with theta-delta slowing.
Action myoclonus consists of arrhythmic muscular jerking induced by voluntary movement. It can be made worse by attempts at precise or coordinated movement (ie, intention myoclonus) and may be elicited by sensory stimuli. The effective stimulus for action myoclonus is thought to be feedback from muscle afferents, although it may be related to activity in the motor cortex relayed to the reticular formation preceding or coinciding with voluntary movement. The condition usually is associated with diffuse neuronal diseases, such as posthypoxic encephalopathy, uremia, and the various forms of peripheral neuroepithelioma, although action myoclonus may be limited to one limb in some cases of focal cerebral damage. It is caused by hyperexcitability of the sensorimotor cortex (ie, cortical reflex myoclonus) or reticular formation (ie, reticular reflex myoclonus), or both.

Autopsied cases have failed to reveal a clear pathology. Theories include loss of inhibitory mechanisms involving serotonin and possibly GABA transmitters. Myoclonus may be seen in degenerative disorders of the nervous system. It may be associated with tonic-clonic seizures or dementia. Myoclonus has been described in cases with Lafora inclusion bodies and cerebral storage diseases, as well as system degenerations: cerebellodentatorubral, pyramidal, extrapyramidal, optic, auditory, posterior columns and gracile and cuneate nuclei, spinocerebellar pathways, motor neurons of cranial nerves and anterior horns, and muscle fibers.

Action myoclonus usually responds to sodium valproate or clonazepam, and some patients with posthypoxic action myoclonus may improve with serotonin precursors.

**Ramsay-Hunt and Unverricht-Lundborg syndromes**

The clinical distinction between Ramsay-Hunt syndrome and Unverricht-Lundborg syndrome (ie, Baltic myoclonus) is unclear because cerebellar signs are found in patients described under both syndromes. Some have proposed that the names could be joined and referred to as Unverricht-Lundborg-Hunt disease. Some authors have suggested that the condition be known as systems degeneration type of progressive myoclonus epilepsy. Presently, the cause of the condition (or spectrum of conditions) is not known.

**Mitochondrial encephalopathy with lactic acidosis and stroke (MELAS) and myoclonus, epilepsy with ragged red fibers (MERRF)**

Isozumi et al described a 50-year-old woman with subacute dementia and myoclonus whose CT scan revealed brain atrophy and EEG revealed PSDs. She initially was thought be suffering from CJD but dramatically recovered over 5 months. Based on further investigations, the final diagnosis was mitochondrial encephalomyopathy. In general, the EEG changes were described as background slowing, multifocal epileptiform discharges, and photosensitivity.

**Poststereotactic surgery**

Patients developed EEG slowing of different degrees about 50% of the time.

**Alpers disease**

This clinicopathological entity, consisting of progressive neuronal degeneration (ie, Alpers disease) of childhood with liver disease, has been studied by Boyd et al. The onset is in early childhood and consists of intractable fits and progressive dementia. EEG studies have been carried out in 12 children with this condition. The EEGs were similar and demonstrated abnormal patterns with high-amplitude, slow activity, as well as smaller polyspikes. The flash VEP was usually abnormal and often asymmetrical. In the appropriate clinical setting, the neurophysiologic features may aid the clinician in diagnosis of this autosomal recessive inherited disorder.

**Adrenoleukodystrophy**

Multifocal paroxysmal discharges, hypsarrhythmic pattern, and prominent arrhythmic delta are present in temporo-occipital areas. Epileptic discharges usually do not occur in adrenoleukodystrophy.

**Zellweger syndrome**

This is characterized by diffuse slowing.

**Infantile neuroaxonal dystrophy**

This condition is characterized by a high-voltage, 14- to 22-Hz activity that is not reactive to environmental stimuli.

**Hallevorden-Spatz disease**

In this disease the EEG is normal to slow.
- **Neuronal ceroid lipofuscinosis**

In the infantile form, the EEG is slow and early, and posterior spikes may be present. Photic response is excessive and evokes high-voltage spikes that are polyphasic. The EEG abnormalities in the juvenile form are not as marked.

- **Gaucher disease**

In patients with type III disease, posterior spikes and sharp waves, diffuse spike and waves, and photomyoclonic and photoparoxysmal responses may be present.

- **Metachromatic leukodystrophy**

Diffuse slowing progresses to high-voltage generalized delta activity. Epileptic activity is rare; however, hypsarrhythmia may be observed.

- **Tay-Sachs disease**

EEG is generally slow. Generalized or multifocal spikes accompany the seizures.

- **Rett syndrome**

This is a progressive encephalopathy observed in girls. Al-Mateen et al reported 15 cases of Rett syndrome. The course is slowly progressive; it occurs only in girls and is characterized by early deterioration of higher brain function with dementia, autistic behavior, loss of purposeful use of the hands, and deceleration of head growth. When affected girls are aged 2-4 years, epilepsy may develop with minor motor seizures. Additional features may include an extrapyramidal disorder with dystonia and choreoathetosis, and lactic acidemia. A precise biochemical marker of this disorder has not been identified.

According to McIntosh et al, Rett syndrome consists of a progressive encephalopathy and psychomotor deterioration in young girls who have appeared clinically normal until age 6-18 months. The incidence is similar to phenylketonuria and autism in females. When the child is at least 6 months old, head growth decelerates in association with severe dementia, autism, apraxia, stereotypic "hand washing" movements, and loss of previously acquired skills. Other signs include breathing dysfunction, seizures, EEG abnormalities, and growth retardation. It appears to be sporadic in occurrence.

The EEG may demonstrate slowing, a variety of nonspecific patterns, and epileptiform discharges. The epileptic activity may include multifocal spikes, slow-wave spikes, and paroxysmal delta slowing with spikes that may appear in sleep; in certain cases, however, sleep may attenuate the EEG abnormalities. Background flattening occurs to some degree, corresponding with the stage of dementia and cognitive decline. Rolandic spikes may be elicited by noise.

**References**

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