1966

Fourteen and six per second positive spike phenomenon as a possible sign of paroxysmal limbic system dysfunction

Joseph Sandsted Henderson
University of Nebraska Medical Center

FOURTEEN AND SIX PER SECOND POSITIVE SPIKE PHENOMENON AS A POSSIBLE SIGN OF PAROXYSMAL LIMBIC SYSTEM DYSFUNCTION

Joseph Sandsted Henderson

Submitted in Partial Fulfillment for the Degree of
Doctor of Medicine.

College of Medicine, University of Nebraska

February 1, 1966

Omaha, Nebraska

TABLE OF CONTENTS

I. Introduction

Since the late 1800's people began to wonder about the function of the brain related to the anatomic origin. In 1890, William James and Lange independently suggested that emotional states (e.g. fear) result from, rather than cause, overt manifestations of emotion. In 1890 Goltz described a dog whose cerebral cortex he had removed. If emotion were expressed by cortical motor areas, none would have been seen in this dog, but the dog did manifest reactions recognized as rage. Thus the apparatus for this kind of emotion was released from inhibitory control exerted by the cerebral cortex. Karplus and Kreidle in 1914 discovered that stimulating the hypothalamic portion of the diencephalon resulted in a variety of visceral responses.

In 1928 Bard made transections which located the neural circuit of rage chiefly to the diencephalon. Their experiments must not be generalized to encompass emotional displays other than rage; it is still not known where all emotional activities originate. In 1937 Papez (27) described a circle of anatomical pathways originating in the so called limbic system which has different definitions by different authors, each including different structures in the brain. The definition of one author is described later in this paper. During its early development certain structures in the brain stem are still immature or have not been exercised enough to maintain homeostasis in the organism.

Motor, sensory, autonomic and reflex pathways are all closely bound together by synaptic pathways, many of which are not traced as yet. Stimulation of areas within the same anatomic structure can produce either inhibitory or stimulatory results: thus an underdeveloped system such as the reticular activating system or the limbic system may cause malfunction of the entire organism or just part of the organism.

In 1951 Gibbs and Gibbs (7) discovered the 14 and 6 positive spike phenomenon. The manifestations that have been found in association with the 14 and 6 per second positive spike phenomenon are multiple; some originating near or in the hypothalamus, some correlation between the anatomical "limbic system" and this phenomenon are thought to exist by some authors.

II. Limbic System

A medial complex of cortex, subcortical nuclei and the tracts which connect them with the hypothalamus and other structures is known anatomically as the "rhinencephalon", literally "nose brain", but according to electrophysiologic studies only a fraction of the rhinencephalon is activated by olfactory stimuli. MacLean (20), to avoid the olfactory implications of "rhinencephalon", has popularized the terms "limbic lobe" or limbic system. First used by Broca to describe this area, "limbic" means border. The cerebral hemispheres arise as an outgrowth from the diencephalon.

The hilus or neck of this growth forms a concentric ring of cerebral cortex which in a sense, is a border of the neocortical vesicle.

As has been stated previously, different authors include different anatomical structures in the "limbic system". The following description is one by Ruch (32). The major part of the limbic system is composed of two rings of limbic cortex and associated subcortical nuclei. The inner ring of three-layered cortex includes the hippocampal formation and is phylogenetically the most primitive, being generally referred to as the "archipallium" or "allocortex". This area includes structures with olfactory connections (the olfactory tubercle, the prepyriform cortex, the periamygdaloid cortex, the corticomedial nuclei of the amygdala) and certain structures and areas which are connected with the thalamus and hypothalamus, mainly the entorrhinal area and the hippocampus. The next ring is designated "juxtallocortex", "mesopallium" or "transitional" cortex; it is homotypical six-layered cortex. This outer ring consists of the cingulate gyrus; and, anteriorly, the orbitoinsulotemporal cortex and, posteriorly, the presubiculum. Two important subcortical masses, the septal nuclei and the basolateral amygdalar nuclei, are associated with the mesopallium. The efferent projection from the mesopallium pass to the subcortical centers, mainly by way of the striatum. The fornix is the main efferent projection for the archipallium, which sends fibers to the septal region, the hypothalamus and the midbrain.

The neopallium subserves some visceral functions, the responsible foci appearing to be discrete, specialized and generally associated with the mesopallium also results in autonomic responses.

In 1937, Papez (27) brought forth his theory of a neuronal circuit concerned with emotion. He stated that pathways occurred between the hippocampus and diencephalon. Activity initiates in the hippocampus and passes through the fornix to the mammillary bodies, then through the mammillothalamic tracts to the anterior thalamic nuclei. Thalamic radiations carry the activity to the cingulate cortex, and then further relays proceeding partly through the cingulum bundle reaching the corpus callosum. The temporo-ammonic tracts of Cajal provides the final pathway to reenter the hippocampus from the entorrhinal area. This report was based on clinical observation and the cerebral lesions that caused abnormal behavior.

Connections between the septum, hippocampus and amygdala to visceral and somatic outflows of the hypothalamus and reticular formation provide a strong anatomical basis for the somatic and visceral manifestations resulting from the ablation and stimulation of these deep limbic structures. As stated by Manter (21), it is clear that the hypothalamus dispatches the antonomic discharge of nerve impulses that produce the physical expression of emotion: acceleration of the heart rate, elevation of blood pressure, flushing (or paller) of the skin, sweating, goose pimpling of the

skin, dryness of the mouth and disturbances of the gastro-intestinal tract. MacLean (20), in 1958, pointed out there is a dicotomy of function between the neocortical and limbic system, but also cautioned that this should not lead to the impression that the two systems work independently of each other. From literature and their findings, Niemer and Speaker (25) believe that the neocortex is anatomically related to the septum, hippocampus and amygdala; these relations provide some basis for the opinion that the neocortex can influence the limbic system and indirectly, therefore, visceral and emotional behavior. Fibers from the gyrus cinguli transmit impulses to other areas of the cortex and produce the emotional coloring of thought which is experienced subjectively during the expression of emotion. If this entire circuit is a reverberatory; it may be possible for impulses to circulate continually and, by reinforcement, cause an emotional experience to be intensified.

Kaada (15) has shown that changes in visceral and respiratory function are caused by stimulating the whole ring of cortex running from the anterior cingulate gyrus across the posterior orbital surface to the insula, the temporal pole, the pyriform cortex, the periamygdaloid and the posterior hippocampal cortex.

Many limbic areas affect the same visceral structure and stimulation of the same point in the limbic lobe will cause several kinds of visceral or vascular responses. In fact, Adey (1) stated

the various segments of the limbic system appear to be closely interrelated, but only poorly connected with the neopallium.

MacLean (20) discovered interrelated areas of the limbic system by applying strychnine to different areas and recording the repetitive discharges electroencephalographically. The responses of limbic structures to stimulation may mean that they serve as a regulatory system for visceral and vascular function superimposed upon the hypothalamus. On the other hand, the responses may mean that the limbic lobe is concerned with emotion. An involvment in emotional expression is suggested by the kind of somatic muscular responses resulting from stimulation in these areas.

The participation of the limbic system in emotion is clearly demonstrated when subcortical limbic structures are stimulated or destroyed, such as the amygdala which is a complex of nuclei with connections with the olfactory bulb and the temporal neocortex. The amygdala also projects to the septal region and the hypothalamus via the stria terminalis. The septal nuclei, rhinencephalic structures lying along the midline just beneath the anterior genu of the corpus callosum, are widely connected with structures known to be concerned with emotion and motivation--the preoptic region, the hypothalamus, the hippocampus, the brain stem tegmentum and the habenulae.

III. 14 and 6 Positive Spike Phenomenon

Gibbs and Gibbs (7) in 1951 first described the 14 and 6 per second positive spike phenomenon. They elaborated on this finding in the Atlas of Electrography (6) in 1952. It was confirmed by Stephenson (35) and Schwade and Geiger (33) in 1955. This pattern is found using the unipolar technique during the transition to sleep. There are groups or "bursts" of positive spikes at frequencies of 13-15 per second and 6-7 per second during deeper sleep, usually bilaterally but independently. In some, the phenomenon occurs during the waking state. It is usually diffuse over the hemispheres, but the highest voltage occurs in the occipital and temporal areas. Sometimes only the 14 per second or the 6 per second pattern is seen; 14 per second positive spikes are more common below twenty years of age and 6 per second positive spikes above forty years of age. The majority, 91%, had the patterns bilaterally, but each discharge is usually confined to one side or the other being independent in the two sides. In 3% the phenomenon was confined to the left and 6% on the right out of 427 patients. In a group of 5,000 epileptics or suspected epileptics, 6% exhibited this phenomenon while only 2% of a group of control subjects exhibited it. Of the 6% only 0.3% showed abnormal activity other than 14 and 6 per second positive spikes while asleep. Metcalf (24) noticed that positive spikes were present in males, but Gibbs and Gibbs noticed no difference in sex.

Poser (30) found the pattern in the sleep record of 312 out of

5,000 known or suspected epileptics and in 8 (2.7%) of 300 control subjects. The awake records of almost all these patients had been normal.

Presthus and associates (31) found this type of electrical complex in at least 38 of 1,463 patients. Only those patients, in whose sleep records the 14 and 6 per second positive spike complex was the only abnormality found, were recorded. Only 18 of his patients were over the age of twenty. His incidence of 2.6% is almost identical to that found by the Gibbs' in their control subjects.

High incidence of headaches (16 patients), dizziness (15 patients), grand mal seizures (14 patients) and gastroentestinal symptoms (8 patients), as well as behavior disturbances, syncope, anxiety, hypersomnia and vasomotor disturbances were recorded by Presthus. In the majority of the patients, their symptoms were paroxysmal in nature.

Encephalitis was diagnosed in 2 of them, 10 had had head injury with concussion and 4 had had injury to the head without concussion.

Kellaway and associates (16) reported on awake and sleep electroencephalograms performed on a series of 950 normal children, in which the 14 and 6 per second positive spike complex appeared in 212%. Records of 200 children showing this pattern all under the age of sixteen were analyzed by Kellaway and associates (18). They stated, "The clinical correlates of the abnormality are primarily

recurrent paroxysmal episodes of autonomic, pain or behavior type... Headaches and/or abdominal pain with associated symptoms of dizziness, weakness, pallor, nausea and vomiting were the most common complaints in our series". They also pointed out that the pattern is not itself a seizure discharge, but a sign of a disorder which may have epileptiform manifestations.

IV. Different Clinical Manifestations of 14 and 6 Positive Spikes

The clinical manifestation correlates are numerous, but there are three general categories that have evolved. They are convulsive equivalents, behavior disorders and convulsive disorders. Convulsive equivalents categorized by Kellaway and associates (17) are as follows: (a) the presence of primary symptoms of headache and/or abdominal pain often with associated pallor, sweating temperature alteration and other autonomic disturbance, (b) the repeated and stereotyped paroxysmal character of the complaint, (c) the presence of 14 and 6 per second positive spiking, (d) the absence of specific disease of abdominal or intracranial structures and (e) a confirmatory criterion of a favorable response to anticonvulsive therapy.

The table on the following page (Table I.) from Gibbs and Gibbs (9) gives the most common manifestations found in this disorder. The following paragraphs discuss individual clinical correlates.

Table I. The incidence of certain symptoms by percent, associated with patients having 14 and 6 per second positive spikes as reported by Gibbs and Gibbs.

	Non-epileptics		Questionable epileptics		Epileptics	
	14 & 6	Control	14 & 6	Control	14 & 6	Control
Headache	46%	34%	48%	34%	25%	18%
Nausea, vomiting	17	12	21	13	13	5
Dizziness	21	13	41	26	7	6
Behavior disorder						
Mild	21	18	15	10	4	8
Severe	10	8	5	3	7	5
Stomachache	9	2	8	8	9	2
Mental deficiency	20	19	7	3	10	5
Blurred vision	7	4	8	5	5	4
Paresthesias	5	2	10	4	9	4
Impaired speech	6	5	1.5	1	2	1
Temper tantrums	10	5	5	.4	4	.5
Rage attacks	3	1	1	.3	1	.3
Psychosis	2	5	.5	.3	.5	.3

(5,165 consecutive patients with 14 and 6 per second positive spikes were matched for age with persons who had normal EEGs from the same referral source)

a. BEHAVIOR:

Wiener (39) has stated that information is information, not matter or energy. It may further be defined as the order that emerges from a background of disorder. In a similar way it may be said that the central nervous system derives information on the basis of changing patterns of neuronal activity. The patterns are of themselves without substance, but they depend on physico-chemical processes within the nervous tissue.

As information is information, not matter or energy, it is obvious that the informational aspects of the psyche defy physical measurement. Communication from one person to another requires some form of behavior. Behavior is, therefore, the physical correlate of information. Behavior may be broadly defined as any change of an entity with respect to its environment. Reasoning from there one can procede and subdivide various forms of behavior into a hierarchical system. The more orderly a form of behavior, the greater its potentiality to convey a greater amount of information.

In their first description of the phenomenon the Gibbs's (7) stated that 19% exhibited rage attacks, and 9% exhibited vicious behavior one of whom committed homicide. Schwede and Geiger (33) described abnormal behavior as, "Sudden outbursts of impulsive, unrestrained, violent behavior vary from relative simple destruction of animate and inanimate objects to the ultimate destructive

forces of murder characterized this large group of 500 patients". Stehle (34) presented his series of patients whose behavior resulted in aggressive assault on people, property damage, fire setting, suicide, homicidal actions or verbalizations and aggressive sexual episodes. Their activity was described as compulsive or impulsive, uncontrolled but well directed, provoked by trivial emotional precipitating factors and regarded by the patient with an inappropriate lack of concern.

b. EMOTION:

On the basis of introspection it is realized that emotion is the only form of psychological information which, short of physical exercise, is associated with extensive behavioral changes inside the body. Information manifest as thought may be derived without an intrusive awareness of bodily feelings. It is the very nature of emotions that they give the sense of pervading the body. Also in contrast to thoughts only, a limited number of emotions can be identified. All the recognized emotions may be considered from the standpoint of self-preservation or to the preservation of the species and to the eradication of their threats, are characteristically "unpleasant" in nature. In this category are fear, anger and sorrow. On the other side are pleasurable emotions that are informative of the removal of threats, the active gratification of needs and the temporary achievement of a state of internal and/or external homeostasis. The emotions of joy and love are examples.

From natural diseases such as epilepsy with foci near or in the limbic system, the amygdalar region for example, a wide variety of alimentary symptoms and vivid emotions such as the feeling of fear, dread, terror and distress can be produced.

c. AUTONOMIC:

Autonomic behavior that may begin with and follow various seizures is characteristically alimentary or of the type required for survival, there may be smacking of the lips, drinking, eating, retching, vomiting or expressions of terror and flight or rage and fight.

Kaada's (15) experiments on animals with chemical and electrical stimulation in the fronto-temporal region have produced many of these manifestations. From the diencephalic region these autonomic changes also can be elicited in animal studies.

d. PAIN:

Kellaway (18) found in his series headaches and/or abdominal pain with associated symptoms of dizziness, weakness, pallor, nausea and vomiting as the most common complaint. Gibbs (7) stated pain as an aura or as a manifestation of a seizure is rare in focal epilepsy unassociated with 14 and 6 per second positive spikes, but as a warning it occurs in 8% and as a seizure in 19% of patients with these patterns. The pain may involve any part of the body mainly the head, but it resembles a sudden onset of trigeminal neuralgia rather than migraine. In some cases the pain

seemed to become continuous and unbearable. If pain is the only symptom, it receives a different diagnosis such as atypical migraine, abdominal migraine, neuritis, displaced intervertebral disc or hysteria.

e. VISCERAL:

If gastric auras and nausea and vomiting are excluded, visceral and vegetative symptoms are not common in the general group of epileptics. Palpitation of the heart, gagging and fever are manifestations of visceral effects, also abdominal pain which may resemble an acute abdomen. Patients do not usually have more than one or two such symptoms and the symptoms tend to recur in each attack. No one autonomic disorder is common, but some type of autonomic disturbance in ictal form occurs in approximately 30% of patients with 14 and 6 per second positive spikes.

Individually this group is interesting because of a close correlation between the presence of 14 and 6 per second positive spikes and a clinical history of episodes of aggressive and destructive behavior.

f. EPILEPTIC SEIZURES:

This phenomenon is found with different types of epilepsy. Only 1/3 of the cases that Gibbs compiled in 1956 (8) were sent in with the diagnosis of epilepsy. The most common major complaint was "pain", next convulsions and then dizzy spills. Epileptic seizures, when present, are most often of the grand mal type.

But many kinds of bizarre seizures are encountered, of special social importance are rage attacks for these sometimes result in homicide. Poser (30) observed in his study of 312 patients with 14 and 6 per second positive spikes that 49% had some kind of convulsion, over 1/3 had fainting spells. Classical petit mal was absent, but 2% had psycomotor seizures. It is chiefly a disorder of adolescents and young adults and may lead to suicidal tendencies with increasing age.

g. NO OVERT MANIFESTATIONS:

This pattern has been encountered in 2% of patients being supposedly normal persons. The symptoms with which it is associated are not properly evaluated in a child, so that a clinical diagnosis is rare in the younger age groups. A few discharges of 14 and 6 per second positive spikes, particularly in children in the absence of clinically evident disorder should not be considered too serious. This pattern may remain asymptomatic and disappear with increasing age. Kellaway's series (15) with control groups gave an incidence of 2.3% average. Ellingson (5) has reported on several sets of twins; one of each pair showed symptoms while the other twin was asymptomatic.

V. Current Concepts and Theories of Origin

Borderlines of epilepsy according to Lennox includes almost anything that falls within episodic neurologic phenomenon. Somers in 1907 wrote a book entitled, "Borderlines of Epilepsy". He

included fainting, vasovagal attacks, tetany, migraine, narcolepsy, sleepwalking and night terrors. Vasovagal autonomic phenomenon and some instances of sleepwalking and night terrors are now proved to be epilepsy. The details of seizures vary so widely that one wonders where epilepsy ends and something not epilepsy begins. Migraine, syncope, hysteria, vertigo and narcolepsy may all be included in borderlines of epilepsy, which seem to be the different manifestations that can be found associated with the 14 and 6 per second positive spike phenomenon.

This phenomenon has been found associated with many etiologic mechanisms. Four gross categories have been found by Poser (30). It may be found in organic damage of the central nervous system, including pre- and perinatal anoxia or traumatic damage, encephalitis, meningitis, vascular anomalies, severe mental retardation associated with neurological signs, lead poisoning in infancy, and intracerebral hematoma and excluding head trauma. It was found that there was a significant difference between those who had only positive spikes and those with associated electro encephalographic abnormalities, the latter being a more frequent finding.

The second category is a history of head trauma, but it is extremely difficult to access the degree of damage to brain tissue.

The third category includes patients with systemic disease such as diabetes, hyper-thyroidism, hepatic coma due to Laennec's cirrhosis, phenoketonuria, pulseless disease and polyneuropathy of

undetermined etiology and patients who were undergoing routine pre-operative study for congenital cardiac abnormalities.

The fourth category is termed idiopathic. The etiology of the disease represented, cannot be determined from the referring physicians histories. This is the largest group and accounts for over one-half of the patients.

The 14 and 6 per second positive spike pattern is believed to be electrical evidence of disordered brain function.

Gibbs and Gibbs (6) suggested the pattern is a sign of an epileptiform disturbance originating in the thalamus or hypothalamus. The Gibbs' based this theory on the character of the EEG abnormality, but no definite experimental work has been done which proves this discharge originates in the diencephalon.

Kellaway (15) believes that unlike the 3 per second spike and wave pattern, this phenomenon does not constitute the seizure pattern itself. They demonstrate this by the fact that the patients showing this abnormality in interictal periods generally show other types of paroxysmal activity, usually hypersynchronous slow at the time of the attack. Therefore, this pattern is a sign of disorder in a particular functional system.

The underlying lesion of which the electrical abnormality is a manifestation apparently is generally epileptogenic in that it usually is associated with clinical and electrical abnormalities of paroxysmal character.

As the 14 and 6 per second positive spike pattern is not in itself a seizure discharge, it cannot be expected to have a clinical correlation of the same degree of specificity for example as the 3 per second spike and wave pattern exhibits. The discharge they believe must be considered more akin to a temporal lobe spike focus, a sign of abnormal activity in a relatively large and complex neuronal system, which could be in the limbic system.

The exact localization of the abnormality discharging area within this structure is the fact in determining the characteristics of the clinical seizure phenomenons which the patient will experience. The ability of the discharge determines whether or not the patient will experience any paroxysmal clinical symptoms.

The great variability of different sites of origin of seizures and the types of seizures produced can be seen from the chart by Penfield in the book by MacDonald (23). The chart (Table II) appears on the following page.

Metcalf (17) suggested that the limbic system was the most likely origin of positive spikes, since Walker and Marshal (37) failed to show positive spikes from implanted electrodes the thalamus or hypothalamus.

VI. The Clinical Significance of the Manifestations Correlating with 14 and 6 Positive Spikes

Walker and Marshal (37) in 1963 reported data derived from surface and depth recording of a patient with 14 and 6 per second

Table II. Sites of origin of epilepsy.

	Clinical Type	Localization
Somatic motor	Generalized (grand mal)	Complete motor
	Jacksonian (local motor)	Pre-rolandic gyrus
	Masticatory	Lower rolandic
	Simple adversive	Frontal
	Tonic postural (decerebrate, opisthotonic)	Brain stem
Somatic sensory (auras)	Somatosensory	Post-rolandic gyrus
	Visual	Occipital
	Auditory	Temporal
	Vertiginous	Temporal
	Olfactory	Infratemporal
Visceral	Autonomic	Diencephalic
Psychical	Dreamy state	Temporal
	Petit mal	
	Automatism (ictal and post-ictal)	
	Psychotic states (secondary)	

positive spikes showing symptoms of periods of amnesia, episodic attacks of uncontrollable sleepy spells and powerlessness. "There is no evidence of any mid-line crossing or interdependence of the 14 and 6 pattern in the cerebral hemispheres, either on the surface or in the depth. The field of '14' component, and of the '6' component overlap in the depths, but are not identical; the '6' field is a little more superficial. There are many 14 and 6 bursts for each example which projects to the surface. Very few project during the waking state while roughly half project during sleep. There is no relationship discernible between sleep spindles and 14 and 6, either in time or in localization within the brain. Thirty six depth electrodes were used but no one point focus were delimited. It appears from the fields observed in depth that a complex conduction pattern is involved."

Hypothalamic thalamic origin of positive spikes was supported by Stephenson (35), who presented two cases of presumptive involvment of deep nuclear structure. Little and Bevilacqua (19) presented a case of a hypothalamic tumor associated with 14 and 6 per second positive spikes. These cases however, may only have associated with the lesion and the pathology was not the cause. Sthele (34) considers the abnormal behavior found by this disease as a result of thalamic dysfunction, which partially or completely interferes with one's ability to adhere to the right instead of the wrong.

Grossman (12) studied responses to auditory stimulation during sleep, and distinguished between the responses of a group of subjects with a history of episodic abnormal behavior and a control group. The normal response consisted of a high voltage biphasic slow wave and a fast wave component, consisting of a constant alteration, usually a decrease in amplitude, of both components in the damaged hemisphere. The change in the abnormal behavior group consisted of a loss of the biphasic activity of the 14 per second wave with an accentuation of the positive phase. The change was transient and shifted from hemisphere to hemisphere, this is the same wave form as the 14 and 6 per second positive spike phenomenon described by Gibbs, but without the 6 per second component.

Grossman stated the difference in the two responses may be explained it the latter responses were a result of transient pathophysiologic disturbances rather than gross structural pathology. He presented evidence (11) which showed that the negative phase of spindles in cats may be abolished by laminar cortical blocking induced by procaine or thermoagglutination, or by surgical slicing of the underlying white matter. One of his conclusions was "reduction of the negative phases of potentials blocking and not by thalamic or hypothalamic excessive neuronal discharge". Another fact brought forth, is that immaturity may be the cause and not an epileptogenic focus that causes the

phenomenon as the high incident age group is young and the postero-temporal region in which many of the spikes are found is late in development. Another suggestion was that the highly skilled and precise aggressive behavior noted by many observers could be explained more easily on the basis of selective partial "laminar decortication" than on the basis of deep lying subcortical disturbances. Subcortical discharge, autonomic manifestations and primitive aggression may be explained as a release phenomenon. Henry (13) in 1963 gave a review of this phenomenon with 107 references. These studies however are very difficult to apply to man as the positive spike phenomenon in lower animals is difficult to produce.

Ellingson (5), in 1963, presented a paper in San Francisco reporting 14 and 6 per second positive spikes in twins and triplets. The first pair were males, age eighteen years. They appeared to be identical, but it was not proven. One twin had episodes of unconsciousness following three football injuries. After the third injury he was confined for several days, two months later he had an episode of confusion lasting about an hour. Five days later, he again became confused. Neurological examination and laboratory tests were negative except for the electroencephalogram which showed 14 and 6 per second positive spikes during sleep. The brother also had 14 and 6 per second positive spike, but was asymptomatic.

The second pair of twins consisted of heterozygous male and female, age seven years. Since they were in a study of serial EEG's, records were taken four hours for the male after birth and five hours for the female after birth. These records were not abnormal. The female had two generalized convulsions associated with an upper respiratory infection several years later. The female was repeated again at six years of age. Waking and sleeping records were taken at 70, 71 and 79 months, neither displayed symptoms of positive spikes, but both had 14 and 6 per second positive spikes on their records.

The triplets were sixteen year old female monozygots, one of which was under emotional stress at home. This one was having blackouts (described as feelings of blankness and loss of support), acute abdominal pain in the right upper and lower quadrants with radiation to part of the upper right thigh, and headaches, usually generalized, dull and "pressurelike". Ellingson inferred from these studies that heredity plays a role in the occurrances of the positive spikes and external factors may precipitate or predispose to the symptoms becoming manifest.

There had been no actual controlled studies relating the clinical correlates with this phenomenon until 1960, when Walter's (38) first double blind study of clinical manifestations associated with this phenomenon was published; previous to this, all studies were retrospective in type with the possibility of error in

observation being greater. These factors may be greatly increased when dealing with symptoms such as outbursts of temper, pain, syncope, headache, pallor or intermittent abdominal pain. All children at one time or another demonstrate these symptoms.

In Walter's (38) study, 75% of the patients had reproducible 14 and 6 per second positive spike patterns in all records, possibly because care was taken to have periods of drowsiness and light sleep.

Four groups of patients were studied; normal EEG, abnormal EEG's, 14 and 6 per second and other electrical abnormalities and those with 14 and 6 per second spiking alone.

The conclusions were: (1) Patients with only 14 and 6 per second spike phenomenon demonstrated less in the way of "emotional symptomatology" than either the normal EEG group, or those with other EEG abnormalities. (2) Patients with 14 and 6 per second activity plus other types of abnormalities demonstrated more "aggressive behavior" than the abnormal or normal EEG. (3) Spiking activity was reproducible in 25% of the patients. (4) There was no evidence of any marked difference in emotional make up between patients with 14 and 6 per second spiking and those of other children referred for EEG's. Other studies conducted recently, Olsen (26), also show less correlation between this phenomenon and behavior or emotional disorders. This study has not received any rebuttals and was acknowledged by Gibbs in 1963 (10).

The length of time during which any one child will show positive spikes is highly variable, the average in Kellaway's (16) series was one to two years regardless of the age at which it was found, but this can vary to seven years or more. The symptoms associated with positive spikes are frequently relieved or improved by anticonvulsive drugs. The best response occurs to those patients whose attacks are paroxysmal in nature. Children who have sudden attacks of headaches, abdominal pain, unexplained destructive behavior or episodic attacks of antonomic dysfunction, clinical seizures including syncopal attacks are also amenable to this type of therapy. Disorders of a continuous behavior abnormality or endocrine dysfunction rarely show good response to therapy. Dilantin, either alone or with phenobarbital has proved the most effective therapy in the majority of their cases. Gibbs and Gibbs (6) in 1952 recommended Dilantin and phenobarbital or Dilantin and Mesantoin in maximal tolerated dosages.

VII. Summary and Conclusion

This paper is a summary of the history of theories of function related to anatomic structure considering one type of EEG phenomenon. The anatomical relationships of the limbic system is presented and also a summary of the original paper by Papez (27), who theorized a possible circuit for the production of emotion in the limbic system.

But despite the anatomically well established connection of the hippocampal formation with the hypothalamus via the fronix and with the anterior cingulate gyrus (area 24) via the mammillary bodies and the anterior nuclei, the emotional significance of these connections as elaborated on by Papez (27) has not been proven. It is quite possible that Papez's system serves the cognative and other subjective aspects of emotion.

Stimulation of relatively large areas of this "limbic system" by different methods has been shown to cause effects on the behavior and emotional reactions of animals and man. The behavior, emotional, pain, autonomic and visceral abnormalities are similar to the clinical correlates of the 14 and 6 per second positive spikes phenomenon found by Gibbs and Gibbs in 1951 (7).

These 14 and 6 per second positive spikes have been called artifactual by some and pathologic by others, many others do not know, but there has been general agreement that this pattern is most likely to be seen in children, adolescents and young adults and that the complexes are always seen during sleep.

This phenomenon is discussed and the different sites of possible origin are also presented, Gibbs' set forth their hypothalamic site of origin, Kellaway presented a diffuse system that is activated in a paroxysmal manner. The current theories of the relationships of this phenomenon with the clinical correlates are also presented, and they may be summarized as follows:

1. A causal or at least causal relationship exists between positive spikes and certain clinical conditions.
2. Some have said that positive spikes are a result of an epileptogenic focus in one of several anatomical location.
3. Association without causal relationship.
4. Other's (Walter #38) have denied any correlation between certain clinical syndromes and positive spikes.

This phenomenon is not an epileptic disease, though the clinical symptoms are paroxysmal in type. The relationships between clinical correlates and this phenomenon have been challenged by a retrospective study by Walter (38), and has not been disputed by Gibbs and Gibbs. This study showed there is no correlation between the phenomenon and the clinical correlates.

The behavior disturbances and different manifestations usually respond to treatment, but after a period of time the medication may by reduced or stopped as this phenomenon in many persons disappears from the EEG and the disturbances may disappear also.

The conclusions drawn are derived from information in the literature, but as yet there is not enough information to derive concrete theories relating the origin of this phenomenon to the anatomic structure of the limbic system.

BIBLIOGRAPHY

1. Adey, W. R., Recent Studies of the Rhinencephalon in Relation to Temporal Lobe Epilepsy and Behavior Disorders, Int. Rev. Neurobiol., 1:1-46, 1959.

2. Arduini, A. and Terzuolo, C., Cortical and Subcortical Components in the Recruiting Responses, Electroenceph. Clin. Neurophysiol., 3:189-196, 1951, (Cited by: Grossman, 1954.)

3. Dutch, S. J., Personal Communication to the Author.

4. Ellingson, R. J., Personal Communication to the Author.

5. _____, Clinical Electroencephalography in Non-Convulsive Disorders of the Brain, Nebr. State Med. J., Vol. 37 180-186, 1952.

6. Gibbs, E. L. and Gibbs, F. H., Atlas of Electroencephalography, Vol. II Epilepsy, Addison-Wesley Press, Inc., 1952, 13:329-345.

7. _____, Electroencephalographic Evidence of Thalamic and Hypothalamic Epilepsy, Neurology 1:136-144, 1951.

8. Gibbs, F. H., Clinical Correlates of 14 and 6 per Second Positive Spikes (1,865 cases), Electroencephalog. and Clin. Neurol. 8:149, 1956.

9. _____, Differentiation of Mid Temporal, Anterior Temporal and Diencephalic Epilepsy: Temporal Lobe Epilepsy, Banner Stone House, C. C. Thomas, 109-117, 1958.

10. Gibbs, F. H. and Gibbs, E. L., Fourteen and Six per Second Positive Spikes, Electroenceph. Clin. Neuro Physiol., 15:553-558, 1963.

11. Gloor, P. and others, A Consideration of Feedback Mechanisms in The Genesis and Maintenance of Hippocampal Seizure Activity, Epilipsia (Amst.), 5:213-238, Sept. 1964.

12. Grossman, C., Laminar Cortical Blocking and its Relation to Episodic Aggressive Outbursts, Arch. Neurol. Psychiat., 71:576-587, 1954.

13. Henry, C. E., Positive Spike Discharges and Behavior Abnormality, (In: Glaser, G. H., EEG and Behavior, New York, Basic Books, Inc., 1963, 315-344.)

14. Hughes, J. R. and others, A Controlled Study on the Behavior Disorders Associated with the Positive Spike Phenomenon, Electroenceph. and Clin. Neurophysiol., Vol. 8 4:349-353, March 1965.

15. Kaada, B. R., Somato-Motor, Autonomic and Electrocorticographic Responses to Electrical Stimulation of 'Rhinencephalic' and other Structures in Primates, Cats and Dogs. A Study of Responses from the Limbic, Subcallosal, Orbito-Insular, Periform and Temporal Cortex, Hippocampus-Fornix and Amygdala, Acta Physiol., Scandinav., (Supp. 83), 24:285, 1951.

16. Kellaway, P. O. and others, A Specific EEG Correlate of Convulsive Equivalent Disorders in Children, J. Pediat. 55:582-592, 1959.

17. _____, Paroxysmal Pain and Autonomic Disturbances of Cerebral Origin, A Specific Electro Clinical Syndrome Epilepsia 1:466-483, 1960.

18. _____, The "14 and 6 per Second Positive Spike" Pattern of Gibbs and Gibbs, Electroenceph. Clin. Neuro Physio. 9:165-166, 1957.

19. Little, S. C. and Vevilacqua, A. R., Dysrhythmia Associated with Proved Hypothalamic Disease, Arch. of Neurol., 6:324-330, 1962.

20. MacLean, P. D., Contrasting Function of Limbic and Neo Cortical Systems of the Brain and Their Relevance to Psycho Physiological Aspects of Medicine, Am. Jr. of Med., Vol. XXV 4:611-626, Oct. 1958.

21. Manter, J. T. and Gatz, A. J., Clinical Neuroanatomy and Neurophysiology, 2nd. Ed., F. A. Davis Company, 1964, Chap. 18.

22. Matthew, J. R. and others, Six and Fourteen Dysrhythmia and the Ego: A Case of Near Homicide, J. Neuro Psychiat., 5:490-494, Dec. 1964.

23. McDonald, J. J., Correlative Neuroanatomy and Functional Neurology, 11th. Ed., Lange Medical Publication, 1962, Pg. 366.

24. Metcalf, D. R., Proceeding of the Eleventh Western Institute on Epilepsy, Milwaukee, Wisconsin, 1959.

25. Niemer, W. T. and others, Neocortico-Limbic Relations in the Cat, Electroencephalog. and Clin. Neurol. 15:827-838, 1963.

28. Pagni, C. A. and others, Some Observations on the Human Rhinencephalon Asterio-electro Encephalographic Study, Electroenceph. Clin. Neurophysiol., 18:260-271, Febr. 1965.

29. Penfield, W. and Kristiansen, K., Epileptic Seizure Patterns, Springfield, Ill., C. C. Thomas, 1951.

30. Poser, C. M. and Ziegler, D. K., Clincial Significance of 14 and 6 per Second Positive Spike Complexes, Neurology 8:904-906, 1958.

31. Presthus, J. and others, Fourteen and Six per Second Positive Spikes: An Electroencephalographic and Clinical Study Preliminary Report, Acta Psychiat. et Neurol. Scandinavia 31:166-167, 1956.

32. Ruch, T. C. and others, Neurophysiology of Emotion and Motivation, (In: Neurophysiology, W. B., Saunders, 1962, Chap. 22.)

33. Schwade, E. D. and Geiger, S. J., Behavior Disorders of the Impulsive-Compulsive Type with Consistent Abnormal EEG Findings, Electroenceph. Clin. Neurophysiol., 7:473-474, 1955.

34. Stehle, H. C., Thalamic Dysfunction Involved in Destructive Aggressive Behavior Directed Against Persons and Property Symposium 14 and 6/sec. Positive Spikes, Electroenceph. Clin. Neurophysiol., 15:160, 1963.

35. Stephenson, W. A., Intracranial Neoplasm Associated with 14 and 6 per Second Positive Spikes, Neurology 1:372-376, 1951.

36. Stevens, J. R., The "March" of Temporal Lobe Epilepsy, Arch., Neurol. and Psychiat. 77:227, 1957.

37. Walker, A. E. and Marshal, C., Depth Recording of the 14 and 6 Pattern Symposium 14 and 6/sec. Positive Spike, Electroenceph. Clin. Neurophysiol., 15:162-163, 1963.

38. Walter, R. D. and others, A Controlled Study of the Fourteen and Six per Second EEG Pattern, Archl, Neurol. and Psychiat. 2:559-566, 1960.

39. Wiener, N., Cybernetics, or Control and Communication in the Animal and the Machine, New York, 1948, John Wiley and Sons, Inc., Paris Hermann et Cie., (Cited by: MacLean, 1958.)