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## Consideration of the clinical correlates of 14 and 6/sec positive spikes

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A CONSIDERATION OF THE CLINICAL CORRELATES  
OF 14 AND 6/SEC POSITIVE SPIKES

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Doctor of Medicine

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## INTRODUCTION

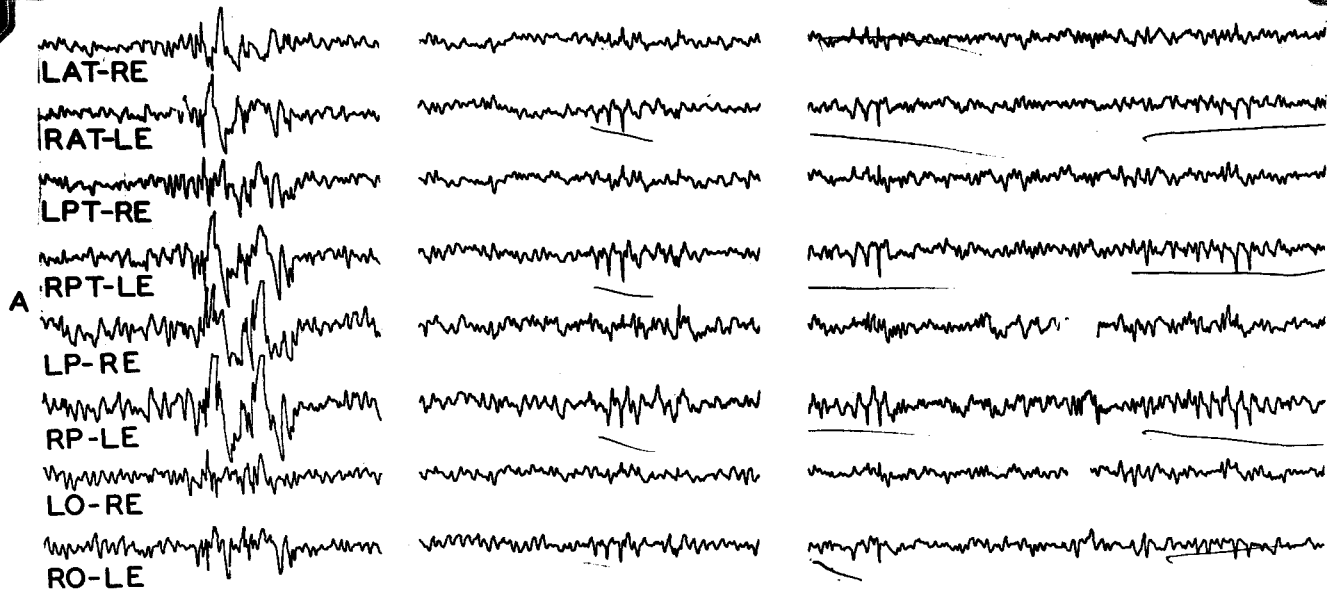
If one records the electroencephalograms (EEGs) of a large number of persons using the unipolar technique (with "active" electrodes on the scalp over active brain tissue and "reference" electrodes over some remote point, usually the earlobes— contralateral earlobe reference electrodes are best), one will occasionally record groups, or "bursts," of positive spikes at frequencies of 13-15/sec and 6-7/sec, widely distributed over the posterior quadrants, but tending to appear independently over the two hemispheres in a random fashion. This phenomenon was first reported by F.A. and E.L. Gibbs (4), and was called by them "14 and 6/sec positive spikes." Fig. 1 shows examples.

The history of the 14 and 6/sec positive spike phenomenon, like that of many newly discovered phenomena of medical interest, has developed through three phases: a descriptive phase, a retrospective clinical correlation phase, and the present phase of controlled studies. The purposes of this paper are (a) to review this development, and (b) to describe a controlled study of the clinical correlates of 14 and 6/sec positive spikes.

At present, most authorities agree about the technique of recording this phenomenon, which was first reported by the

Fig. 1. A. EEG showing 14 and 6/sec positive spikes (predominantly 6/sec) during light sleep in a 16 year old white female with a history of feelings of "blankness" and "loss of support," acute abdominal pain in the right upper and lower quadrants, and headaches. Complete physical and neurological examinations, blood and urine analyses, CSF analysis, skull x-rays, IVP, BE, and UGI series have all been negative on several occasions.

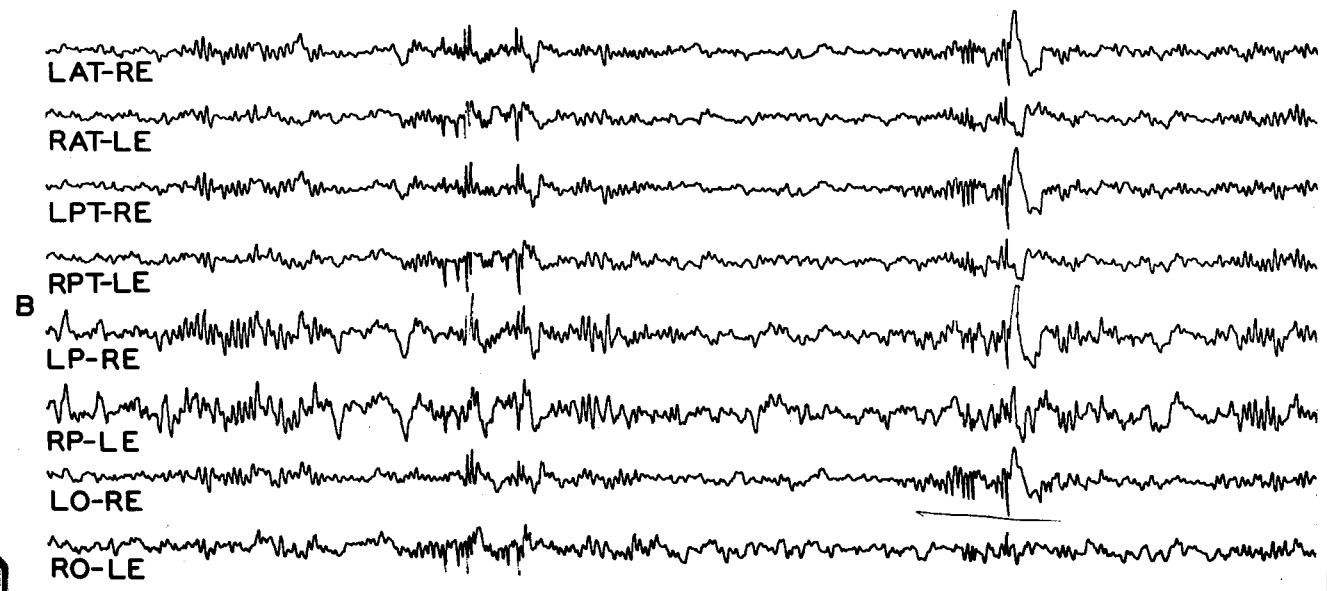
B. EEG of asymptomatic identical sibling showing predominantly 14/sec positive spikes. The third triplet also showed 14 and 6/sec positive spikes; she too was asymptomatic.



SEC

100LV

AGE 16



Gibbses in 1951. They stressed (a) the importance of using unipolar recording technique and (b) that the phenomenon is usually seen only during the wakefulness-asleep transitional state. They described the phenomenon as consisting of 14/sec positive spikes, which most commonly appeared at the level of light sleep, and 6/sec positive spikes, which most commonly appeared at a deeper level of sleep. The spikes usually occurred bilaterally but independently in the two hemispheres. They are rarely restricted to one lobe, are usually diffuse throughout one hemisphere with no predilection for either hemisphere, and are usually of the highest voltage in the occipital area. Sometimes only one frequency (14 or 6/sec) is seen, and a higher incidence of unilateral distribution has been noted when only 6/sec positive spikes are seen. No sex differences were reported in the early papers.

In a later paper (8) Gibbs and Gibbs described the chronological development of 14 & 6/sec positive spikes. They stated that the 6/sec frequency is more common during the first year of life. The 14/sec frequency, either alone or in combination with the 6/sec frequency, is more common from 1 year to 40 years, after which the 6/sec frequency is again more common. Young children exhibit the phenomenon in deep sleep, older children

exhibit it in light sleep, and adults more commonly exhibit it in a waking state.

Further analysis by the Gibbises revealed that 6% of a group of 5,000 epileptics or suspected epileptics exhibited this phenomenon while only 2% of a group of 300 control subjects exhibited it. Of the 6%, only 0.3% had any type of seizure discharge while awake and 2% showed abnormal activity other than 14 and 6/sec positive spikes while asleep. The phenomenon was observed predominantly in adolescents and young adults.

Retrospective clinical correlation revealed that preliminary diagnoses included epilepsy 65%, (46% grand mal, 14% atypical, 2% psychomotor, 2% focal, 1% Jacksonian, and 0% petit mal), syncope 16%, neurosis 15%, post-traumatic syndrome 16%, post-encephalitic syndrome 11%, hysteria 10%, psychopathy 9%, behavior disorder 7%, and psychosis 5%. Major symptoms included generalized convulsions 46%, syncopal attacks 36%, attacks of pain 20%, attacks of numbness and paresthesias 19%, attacks of rage 19%, antisocial and vicious behavior 9%, attacks of nausea and vomiting 9%, vasomotor attacks 8%, sleep attacks 6%, mental deficiency 4%, and crying spells 4%. Symptom complexes included convulsions 49%, disorders of body sensation 39%, syncopal



attacks 36%, ictal vegetative symptoms 30%, ictal disorders of emotion and emotional expression 28%, and attacks of sleep 6%. Presumptive etiology included head trauma 20%, encephalitis 7%, birth injury 3%, vascular accident 1%, and carbon monoxide poisoning 1%. The disorders usually responded well to Dilantin and Mesantoin.

The incidence of several prominent symptoms presented in the Gibbsses' (8) most recent article is listed in Table I along with the control group incidence.

Gibbs and Gibbs concluded that 14 and 6/sec positive spikes are a distinct electroencephalographic entity composed of distorted sleep spindles, both because they do not correlate highly with other types of seizure discharges or other electroencephalographic abnormalities, and because they occur most commonly in the adolescent and young adult age group. They further stated that this phenomenon is indicative of a distinct type of epilepsy because of the high incidence of pain symptoms, the specificity of visceromotor and vegetative symptoms as opposed to vague auras, the high incidence of vegetative and thalamic symptoms, the lack of a temporal association of seizures with the spikes, symptomatic differentiation from psychomotor epilepsy in that

assaultiveness, when it occurs, is highly skilled and well executed, and the higher incidence of an emotional precipitation of seizures. They also postulated that the positive spikes were of thalamic and hypothalamic origin because recent studies (16,22, 23) suggest that sleep spindles are of thalamic and hypothalamic origin, the discharges are of a diffuse but lateralized distribution, the discharges are of a positive nature, and because the symptom complexes are suggestive of thalamic-hypothalamic disorders.

During the twelve years following the Gibbises' first papers there have been a large number of contributions to the literature dealing with 14 and 6/sec positive spikes. Henry (11), in his comprehensive review of the subject in 1961, lists 107 references. Only the more significant papers will be reviewed here to elucidate the pertinent areas of controversy.

The bulk of the literature is in agreement with the Gibbises' description of the phenomenon and their proposition that 14 and 6/sec positive spikes are a distinct electroencephalographic entity. However, Hughes (12), after careful frequency analysis of the positive spikes in 38 patients, found that the slower frequency was actually 7/sec. He stressed the neurophysiologic significance of

this finding, stating that the harmonic relationship of the frequencies (14 and 7/sec) suggests involvement of a specific neuronal system.

The clinical correlates of 14 and 6/sec positive spikes reported in retrospective studies are quite diverse and vary with the interests and referral sources of the laboratory involved. However, there are certain broad groups of clinical correlates which are repeatedly re-emphasized, including convulsive equivalents, behavior disorders, and convulsive disorders.

The most specific description of convulsive equivalents was offered by Kellaway et al (14). They established the following criteria: (a) the presence of primary symptoms of headache and/or abdominal pain, often with associated pallor, sweating, temperature alteration, and other autonomic disturbances, (b) the repeated and stereotyped paroxysmal character of the complaint, (c) the presence of 14 and 6/sec 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.

Although many of the earlier contributions to the literature did not describe these symptoms so precisely, many have alluded

to their presence. Gibbs and Gibbs, in their second, and more elaborate, presentation of this subject (7), noted the high percentage of atypical seizures with distinct characteristics of pain, paresthesias, vegetative symptoms, and syncopal attacks. Kellaway et al. (13), in an earlier study, reported that 53% of their subjects exhibited convulsive equivalent disorders and that partialing out other electroencephalographic abnormalities did not statistically alter this percentage. Several of their subjects who exhibited 14 and 6/sec positive spikes following head injury or encephalitis, but who did not originally exhibit convulsive equivalent disorders, later developed these disorders. However, other subjects displayed the clinical disorder before the positive spikes became manifest. Many of their subjects who exhibited behavioral or convulsive symptoms also exhibited convulsive equivalent disorders. Poser and Ziegler (26) reported a 20% incidence of convulsive equivalent disorders and a 3% incidence of histories suggestive of migraine headaches. Millen (20) reported that 39.3% of 185 clinical cases presenting a chief complaint of abdominal pain syndromes exhibited 14 and 6/sec positive spikes. Sheehy et al. (30) stated that 14 and 6/sec positive spikes were a significant finding in "abdominal epilepsy" and were, in fact, one of the main criteria

in its differential diagnosis from abdominal migraines. They also found that abdominal epilepsy was a benign syndrome usually easily controlled with anticonvulsive therapy.

In addition to convulsive equivalent disorders, a large number of laboratories reported certain characteristic behavioral disorders to be associated with positive spiking. It was stated above that 19% of the group of patients first described by the Gibbises exhibited rage attacks and 9% exhibited vicious behavior, one of whom committed homicide. A characteristic description of the type of behavior thought to be exhibited by some patients with positive spikes was presented by Schwade and Geiger (28) in their report on 500 subjects with 14 and 6/sec positive spikes associated with abnormal behavior. "Sudden outbursts of impulsive, unrestrained, violent behavior vary from relatively simple destruction of animate and inanimate objects to the ultimate destructive forces of murder characterized this large group of patients." Schwade and Geiger (27) earlier described in detail a case of matricide and Schwade and Otto (29) presented a case of probable multiple homicide. Woods (36), in a review of the behavioral aspects of positive spiking in 1961, stated that there were at least ten murders associated with 14 and 6/sec positive spikes. Stehle (31) presented a series of patients exhibiting

positive spikes whose behavior resulted in serious physical damage to others, extreme property damage, fire setting, homicidal actions or verbalizations, suicidal attempts, aggressive sexual episodes, and five deaths. He described their behavior 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. He also stated that this behavior was a result of thalamic dysfunction, which partially or completely interfered with one's ability to adhere to the right instead of the wrong, although the difference between the two and the consequences of the acts were realized. An account of two teenage murderers with 14 and 6/sec positive spikes was even published in Time magazine (33).

The third general class of clinical correlates of 14 and 6/sec positive spikes is that of typical epileptic seizures. The Gibb's original presentation of this aspect was described earlier in this paper. Kellaway et al. (13) found 30% incidence of seizures, 38% of which were generalized convulsions and 62% of which were attacks of unconsciousness, in his series of patients who exhibited 14 and 6/sec positive spikes as the only electroencephalographic abnormality. This incidence was essentially unchanged if those

patients which exhibited nonspecific electroencephalographic changes in addition to 14 and 6/sec positive spikes were added. The incidence of seizure was higher among those patients who exhibited both focal signs and positive spikes, and 73% of those patients who exhibited paroxysmal generalized spike-and-wave patterns in addition to positive spikes had clinical histories of seizures. Poser and Zeigler (26) reported that 42.6% of patients with grand mal or psychomotor epilepsy also exhibited positive spikes. They noted a significant lack of correlation with petit mal epilepsy which agrees with the observation of Gibbs and Gibbs (8), who presented in their latest publication, the following percentages of 14 and 6/sec spikes in several types of seizures: "atypical" (682 cases) 68.4%, focal (342 cases) 41.4%, grand mal (3609 cases) 39.8%, febrile convulsions (259 cases) 15.2%, petit mal (823 cases) 9.4%, and psychomotor (250 cases) 7.5%. They stated that the 14 and 6/sec positive spike and the "petit mal" spike-and-wave complex are more rarely associated with one another than with other types of seizure discharge, and that the 14 and 6/sec positive spike pattern was less frequently associated with petit mal seizures than in the general population.

In addition to the three general classes of clinical correlates listed above, there are several other observations which are

pertinent to this discussion. Several investigators (9,11,24,26) noted that the appearance of 14 and 6/sec positive spikes could be predicted from the clinical history presented. Others (15,19) noted a higher incidence of 14 and 6/sec positive spikes among psychiatric patients than in "normals" or other types of patients. Millen (21) presented a case history of five year old identical twins, who both suffered with recurring, episodic, intermittent attacks of abdominal pain, associated with anorexia, nausea, and vomiting. Both patients showed 14 and 6/sec positive spikes in each of two EEG records. All other family members had normal electroencephalograms, but gave the following clinical histories. The 38 year old mother suffered from migraine headaches since birth. The 38 year old father had had, as a child, abdominal pain episodes similar to those of his children. An 18 year old brother suffered from episodic abdominal pain for several years during adolescence. This study is certainly suggestive of a possible hereditary factor. Ellingson et al. (5) reported 14 and 6/sec positive spikes in two sets of twins and one set of triplets. The first pair were apparently identical 18 year old white male twins, but monozygosity was not proven. One of the boys exhibited episodic periods of transient unconsciousness followed by confusion. These attacks followed three football injuries with cerebral concussion,



and became progressively more severe. All examinations were negative, except the electroencephalogram which showed 14 and 6/sec positive spikes. His brother, who was asymptomatic, and denied previous head injury, also showed 14 and 6/sec positive spikes. The second pair consisted of 7 year old heterozygous twins. The female had two generalized convulsions at 11 months of age. Electroencephalograms were taken at 4 and 5 hours of age, male and female; 4 days, female; 6 years, male and female waking record; 70, 71, and 79 months, male and female waking and sleeping records. At 70, 71, and 79 months both male and female exhibited 14 and 6/sec positive spikes. Neither displayed any of the symptoms commonly associated with positive spikes. The triplets were 16 year old female monozygots, one of which had a history similar to Kellaway's convulsive equivalent state, and who had been under emotional stress. All three exhibited 14 and 6/sec positive spikes although the other two girls were asymptomatic. The 38 year old mother, who had developed generalized convulsions during a spontaneous menopause at age 32, exhibited one burst of 6/sec positive spikes. Ellingson et al. inferred from these studies that heredity may play a role in the occurrence of positive spikes and that the exogenous factors, such as head trauma and cerebral infection, may be contributory or precipitating causes of the symptoms.

A major area of controversy provoked by the Gibbsses' presentation of their work on 14 and 6/sec positive spikes concerns the anatomical origin of the phenomenon. The bases of their theory that 14 and 6/sec positive spikes are of subcortical origin, which were presented earlier in this paper, received much criticism. Although the present evidence suggests that sleep spindles are of hypothalamic or thalamic origin, no conclusive evidence has yet been presented (4). In addition to this, there is no conclusive evidence that positive spikes are necessarily distorted sleep spindles. The diffuse and lateralized distribution of the discharges is suggestive of a subcortical origin but not necessarily thalamic or hypothalamic. The theory that the positive sign of the spikes at the point of detection is indicative of a subcortical origin has been effectively criticized by Bishop (2). Finally, while symptom complexes associated with 14 and 6/sec positive spikes are suggestive of thalamic or hypothalamic origin, they may also be produced by stimulation of other areas of the brain (4), including the so-called limbic system.

Grossman (10), in his studies of evoked responses to auditory stimulation during sleep, distinguished between the responses of a group of known brain damaged subjects and a group of subjects with a history of episodic abnormal behavior. The normal evoked

response consisted of a high voltage biphasic slow wave and a fast wave component, consisting of a train of 14/sec, biphasic, sinusoidal oscillations. The variation of this pattern in the brain damaged group consisted of a constant alteration, usually a decrease in amplitude, of both components in the affected hemisphere. The changes in the second group consisted of a characteristic loss of the biphasic activity of the 14/sec wave with an accentuation of the positive phase. The change is transient and shifts from hemisphere to hemisphere and is in fact the same waveform as the spontaneous 14 and 6/sec positive spike described by Gibbs without the slow component. Grossman proposed that the difference in these two responses might be explained if the latter responses were a result of transient pathophysiologic disturbances rather than gross structural pathology. He then emphasized that the important aspect of the question of the origin of positive spikes was not that of determining the origin of the 14/sec sleep spindles but rather of determining the origin of the change in the biphasicity of these spindles. To further elucidate the possible origin of this change Grossman presented experimental evidence of his own and others (1,3,25) which showed that the negative phase of spindles in cats may be abolished by laminar cortical blocking induced by cocaine, thermagglutination, and procaine. In one of the

experiments related, the subcortical influence was blocked by undercutting the underlying white matter. Grossman concluded that "reduction of the negative phases of potentials is most likely produced by an intracortical blocking and not by thalamic or hypothalamic excessive neuronal discharge." He further supported these experimental data by suggesting that immaturity rather than an epileptic focus may be involved, in view of the high incidence of positive spikes in the younger age group and the topographical distribution of positive spikes in the posterotemporal association region, which is late in ontogenetic development. He further suggested that the highly skilled and precise aggressive behavior noted by many observers could be more reasonably explained on the basis of selective partial "laminar decortication" than on the basis of deep-lying subcortical disturbances. That is, the excessive subcortical discharges, autonomic manifestations, and primitive aggression may be explained as a release phenomenon.

However attractive this theory might be, it is important to note that, although positive spikes may be produced by such experimental manipulations in cats, it does not necessarily follow that the same mechanism is involved in human patients.

Walker and Marshall (34) presented the following information gained from extensive surface and depth recording on a patient exhibiting 14 and 6/sec positive spikes who was referred for episodic attacks of uncontrollable sleepy spells, powerlessness, and periods of amnesia.

"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 depths. The field of the '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 was delimited. It appears from the fields observed in depth that a complex conduction pattern is involved."

Metcalf (18) suggested from this then unpublished study that the limbic system was the most likely origin of positive spikes, since Marshall and Walker failed to show positive spikes from implanted electrodes in the thalamus or hypothalamus.

The hypothesis of the hypothalamic-thalamic origin of positive spikes was supported by two independent studies relating the incidence of this phenomenon to proved hypothalamic-thalamic pathologic processes. Stephanson (32) presented two cases of

presumptive involvement of deep nuclear structures with 14 and 6/sec positive spikes. Little and Bevilaqua (17) presented a case of proved hypothalamic tumor associated with 14 and 6/sec positive spikes. It should be noted, however, that the association may have been coincidental. Direct anatomical studies in humans can only be performed on the few patients who are either surgical problems or come to autopsy, and who may not be typical.

Finally, we come to the subject of controlled studies; an area in which there is a regrettable paucity of information. In fact, there is only one adequately controlled study in the literature, that of Walter et al. (35). They observed that the studies up to the time of their investigation were largely retrospective in nature, and made the following comment:

"Though this methodology is a traditional and useful one in many investigations, certain defects are often apparent. Errors of observation may be greater unless well-controlled comparisons with other groups are made, and unless devices are used to reduce the inherent bias of the participants in the study. These factors may be more operative when one is dealing with symptoms such as outbursts of temper, intermittent abdominal pain, headaches, pallor, and syncope. All children may at one time or another demonstrate these symptoms."

To minimize this inherent bias, a controlled study was done with 74 patients between the ages of 5-20, all of whom were referred

for symptoms possibly related to the central nervous system. Each subject was examined by a neurologist, a psychiatrist, and a psychologist, none of whom were aware of the electroencephalographic classification. The mothers of the patients were evaluated by one of the two psychiatrists and by the psychologist by means of the MMPI. All observations were recorded independently by each observer on a list of 263 items coded for IBM analysis. The 74 patients were divided into four groups (approximately matched for age and sex) according to their electroencephalographic classifications of normal, abnormal, mixed abnormal and 14 and 6/sec positive spikes, or pure 14 and 6/sec positive spikes. The groups were then compared in relation to five basic symptom complexes obtained from the extensive psychiatric, psychometric, and neurological examinations. The symptom complexes were aggressive behavior, organic symptomatology, emotional symptomatology, disturbed mother syndrome, and disturbed family syndrome. Out of the 80 possible combinations for four groups and five symptom complexes, only two comparisons yielded statistically significant differences at the 5% level of confidence. The mean score of the pure 14 and 6/sec positive spike group was statistically lower than either the normal or abnormal group regarding emotional symptomatology and the mean

score of the mixed 14 and 6/sec positive spike group was significantly higher than either the normal or abnormal groups regarding aggressive behavior. Since in making 80 statistical comparisons using the 5% level of confidence one would theoretically expect that by chance alone 4 differences would appear to be significant, 2 in the predicted direction and 2 in the opposite direction, and since in this study 2 differences appeared to be significant, one in the predicted direction and one in the opposite direction, it is clear that the results of this study may be taken to be entirely negative.

Each group was also compared with every other group on the occurrence of headaches, abdominal pain, and vertigo with no statistical differences found. The writers concluded, "In our study we were unable to confirm the association of autonomic phenomena with 14 and 6 per second abnormality." In reference to behavioral differences they stated:

"This was an attempt to determine whether there was something unique about the personality of the child with 14 and 6 cps abnormality. We were unable to find any outstanding area of significant difference between these children and the other groups studied. It may be true that children with 14 and 6/sec abnormality are more likely to have behavior disturbance than children in the general population. However, we found little evidence that their emotional make-up was markedly different from that of other children referred for EEGs."



The most surprising aspect of the Walter study is the lack of criticism it received. Gibbs and Gibbs (8) mentioned "one dissenting study to date" in their latest review of the subject, but offered no rebuttal. Henry (11) offered the opinion that a "clinically normal" group of children should have been included. However, to include "normal" children would contribute an uncontrolled variable since they would not be from the same referral source. One other point of interest is the high incidence of "organic" diagnoses as opposed to functional psychiatric diagnoses in both the mixed 14 and 6/sec positive spike group (81.25%) and the pure 14 and 6/sec positive spike group (38.57%). This is different from other studies, and is most likely a function of referral source, as mentioned earlier.

The investigation described in the following pages is an attempt to add another controlled study of the 14 and 6/sec positive spike phenomenon and its clinical correlates.

## METHODOLOGY

The subjects for this experiment were obtained from the 4,921 referrals to the EEG Laboratory of the Nebraska Psychiatric Institute (NPI) from October 10, 1957, through September 30, 1963. This laboratory receives referrals from NPI, (adult, childrens, and mental retardation inpatient and outpatient services), all services of the University of Nebraska Hospital, and the University of Nebraska Outpatient Clinics.

EEGs had been recorded on an 8-channel Offner Model D-4 or 8-channel Grass Model III or Model 6 Electroencephalograph. Surface disk electrodes were applied bilaterally with Bentonite paste to the frontal (RF and LF), the anterior and posterior temporal (RAT, LAT, RPT, and LPT), the parietal (RPC and LPC), the occipital (RO and LO) areas of the head and to the earlobes (RE and LE). All waking-sleep transitional periods were recorded using unipolar montages with the reference electrodes on the homolateral or contralateral earlobes (usually contralateral).

An Experimental Group of patients was selected on the basis of having displayed 14 and/or 6/sec positive spikes on one or more records. All of the records originally classified for clinical use

were re-examined by the electroencephalographer to ascertain the reliability of the original classifications. Five original patients were omitted because of the equivocal appearance of their positive spikes. The remainder were subclassified according to the location and frequency of the positive spikes and the presence or absence of other electroencephalographic abnormalities. There were 104 patients in the Experimental Group.

Two control groups were also selected from this same referral source, a General Control Group and a Matched Control Group. The General Control Group was composed of all the patients in this time period whose EEGs contained a recording of a waking-sleep transition minus those showing positive spikes. The Matched Control Group (N=104) was composed of patients who were matched for age and sex with the patients in the Experimental Group. These patients were selected as follows. Each patient with 14 and/or 6/sec positive spikes in his EEG was paired with the next patient (alphabetically) in the EEG name file, who was of the same age and sex, and who had had a normal EEG recorded during the period from October, 1957, through September, 1963, including recording during the waking-sleep transition period using a unipolar montage, and having at no other time displayed an abnormal EEG.

The purpose of the General Control Group was to provide a comparison with the Experimental Group on the factors of age and sex, since these factors were held constant between the Experimental and Matched Control Groups. The purpose of the Matched Control Group was to provide a comparison with the Experimental Group on the factors of clinical complaints and diagnoses, with the factors of age, sex, and (it was hoped) referral source held constant, the experimental variable being presence or absence of 14 and/or 6/sec positive spikes in the EEG.

A check sheet was prepared on which were listed the complaints most often presented by patients displaying 14 and/or 6/sec positive spikes (as compared with subjects not displaying them) derived from the tables and charts published by Gibbs and Gibbs (1963). See Table I, pg. 6.

The medical chart of each patient in the Experimental and Matched Control Groups was reviewed by the investigator, who rated the presence or absence of each complaint (and in some instances the degree of severity of the complaint) on the check sheet by the forced choice method. The patient's diagnosis was also recorded in each case. These operations were performed "blind," i. e., the investigator was not aware of which group the patient was in at the time he made his judgments, and the charts of the two groups were presented to him in a random order.

## RESULTS

Of the 104 subjects included in the Experimental Group, 32 had had more than one EEG recording which included the waking-sleep transition. Of these, 13 subjects exhibited positive spikes in both or all records and 19 subjects failed to exhibit positive spikes in one or more records. Of 1,716 EEGs containing a recording of the waking-sleep transition, 124 or 7.2% contained positive spikes.

The sex distribution of the Experimental and General Control Groups is as follows: Experimental - males=72 (69%), females=32 (31%); General Control - males=919 (58%), females=673 (52%). This difference is significant at the 5% level of confidence (Chi-square test).

The age distributions of the Experimental and General Control Groups are shown in Table II. The difference between the distributions is significant at the 0.1% level of confidence. This difference is greatest in the age range of 5-20 years, which contains 87% of the Experimental Group as opposed to 51.6% of the General Control Group. The percentage of the total EEGs with a waking-sleep transition showing positive spikes in this age range is 11.7%.

In Table III are shown the age distributions according to sex

Table II. Age Distribution at Time of EEGs of Experimental (E) and General Control (GC)

Groups.

	0-4	5-9	10-14	15-19	20-29	30-39	40-49	50-59	60-69	70
E	7	31	37	41	5	3	0	0	0	0
GC	194	313	255	255	219	120	112	78	30	16

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Table III. Age Distribution of Subjects in Experimental Group According to Sex.

	0-4	5-9	10-14	15-19	20-29	30-39
M	5	19	26	20	1	1
F	1	6	5	15	3	2

of the subjects in the Experimental Group. The difference between the distributions is significant at the 5% level of confidence. It will be noted that the modal interval for males is 10-14 years of age and for females is 15-19 years of age.

The topographical distribution and frequencies of the positive spikes exhibited by patients of the Experimental Group are shown in Table IV. Those subjects showing three or fewer bursts were not included because it was felt that there was not sufficient information for localization or lateralization of the positive spikes.

Of the 104 Experimental patients, 73 had otherwise normal EEGs. The remainder displayed other abnormalities, in addition to positive spikes, as follows: 11 diffuse slow, 5 bioccipital slow, 1 focal slow, 5 diffuse seizure discharges, 8 focal seizure discharges, and 1 interhemispheric asynchrony. Two patients had more than one EEG abnormality in addition to positive spikes.

The comparison of the Experimental and Matched Control Groups with respect to diagnoses and symptoms are listed in Tables V and VI respectively. In addition to being matched for age and sex, the groups were approximately matched for the specific referral sources which are listed in Table VII. The only significant difference between the two groups was that of an increased incidence

Table IV. Topographical Distribution and Frequencies  
of Positive Spikes in Patients.

Topographical Distribution	Frequencies of Positive Spikes		
	14 & 6	14 only	6 only
Bilateral	57	13	6
Left Side Only	1	1	2
Right Side Only	2	3	3



Table V. Frequency of Diagnoses of Experimental (E)  
and Matched Control (MC) Groups.

	E	MC
None	15	13
Mental Deficiency	17	17
Epilepsy	7	4
Other Neurological	16	15
Personality Disorder	30	21
Adjustment Reaction of Adolescence	11	8
Adjustment Reaction of Childhood	19	11
Neurosis	12	10
Psychosis	4	18
No Psychiatric Diagnosis	0	2
Medical-Surgical	5	3

Table VI. The Frequency of Recorded Symptoms in  
Experimental and Matched Control Groups.

	E	MC
Headache	18	15
Dizziness	12	7
Nausea	4	2
Vomiting	5	2
Behavior Disorder	35	37
Stomachache	8	3
Mental Deficiency	29	24
mild	18	10
moderate	7	10
severe	1	3
undetermined	3	1
Blurred Vision	6	4
Paresthesias	2	0
Impaired Speech	20	21
Temper Tantrums	17	19
Rage Attacks	10	15
Seizures	27	28
psychomotor	3	2
grand mal	8	3
petit mal	3	0
febrile	3	10
Jacksonian	0	1
atypical	6	8
undetermined	4	5

Table VII. Referral Source of Experimental (E) and  
Matched Control (MC) Groups.

	E	MC
NPI	77	77
UNH	5	7
UND	22	20

of a diagnosis of psychosis in the Control Group. The difference was significant at the 0.1% level of confidence.

The bulk of the undiagnosed patients were found in the University of Nebraska Clinics whose records contained diagnostic impressions (many of which were different from week to week and clinic to clinic) but no final diagnoses. One example of the discrepancies which may result from this inadequacy is that although 13 EEGs of the Experimental Group showed generalized or focal seizure discharges only 7 official diagnoses of epilepsy were made. However, this discrepancy is somewhat less than it would first appear if one considers that 3 of the subjects had had febrile convulsions.

## DISCUSSION

In discussing the general characteristics of the EEGs containing 14 and/or 6/sec positive spikes and the comparison of the Experimental and General Control Groups in terms of age and sex distribution there are several points worthy of attention. The fact that 19 of the 32 subjects who had had repeat EEGs did not show positive spikes on one or more records is consistent with the findings of others reported in the literature. Further, the finding is what one could expect if 14 and 6/sec positive spikes were

seizure discharges, since epilepsy is by nature a paroxysmal disorder, and seizure discharges in the EEGs of epileptics tend to come and go from time to time. However, it has been noted by numerous investigators that positive spikes are not temporally associated with seizure phenomena and are probably not seizure discharges per se.

The topographical distribution and frequencies of the 14 and 6/sec positive spikes exhibited by our group are consistent with data reported by other investigators, as is the observation that diffuse slow and bioccipital slow abnormalities are those most commonly associated with 14 and 6/sec positive spikes.

The high incidence of positive spikes in the age range of 5=20 years is consistent with reports by other investigators. The percentage of records containing a waking=sleep transition showing 14 and/or 6/sec positive spikes (7.2% of all records and 11.7% of records in the 5=20 year old group) is somewhat lower than reported by some investigators. However, there is a wide range of percentages reported in the literature and, at the present time, no norm has been agreed upon.

The higher incidence of 14 and 6/sec positive spikes in males (as exhibited by our group) is another variable finding in the literature. Gibbs and Gibbs reported no sex difference while others (19)

have reported a higher incidence of males.

The significance of the earlier appearance of positive spikes in males (modal interval of 10-14 years of age) as compared with females (modal interval of 15-19 years of age) is not yet known. No other investigators have reported this difference, but no others appear to have made the necessary comparison of males and females with respect to age distribution.

We have seen in the introduction that a large number of investigators held (explicitly or implicitly) that a causal or at least casual relationship exists between positive spikes and certain clinical conditions. Some have gone so far as to state that positive spikes are a result of an epileptogenic focus in one of several specific anatomical locations. Others have commented on possible associations of positive spikes and clinical syndromes but have cautiously avoided proposing a causal relationship. The only prospective study to date failed to show any significant correlation between certain clinical syndromes or symptoms and positive spikes (35).

Our study (designed to partially eliminate the inherent bias of a retrospective study by the "blind" examination of clinical charts and a forced choice check list) failed to show any significant

difference between the Experimental and Matched Control Groups, except for a larger incidence of a diagnosis of psychosis in the Matched Control Group. The data listed in Table VI cannot be directly compared with the data of Gibbs and Gibbs summarized in Table I because our data is not subdivided into three groups comparable to those of the Gibbsses and the Gibbsses do not give enough information to combine their data into one group. A difference in referral source must also be considered. It is interesting to note, however, that in the Gibbsses' non-epileptic group there is a higher incidence of psychosis in the group without 14 and 6/sec positive spikes than in the group with 14 and 6/sec positive spikes.

The data of this experiment does not support the hypothesis that a relationship (causal or casual) exists between the presence of symptoms (commonly associated with positive spikes) in the clinical records of patients referred to the NPI EEG Laboratory. It should be noted that absence of a symptom on a clinical record does not necessarily mean that the patient did not have these symptoms since the physician may have neglected to record the symptom or the patient may have neglected to mention the symptom. However, if a discrepancy of eliciting or recording these symptoms did exist between the Experimental and Matched Control Groups, it is more likely that an adequate history of these symptoms would

have been recorded on the Experimental Group since the physician, who was aware of the EEG classification, would be more likely to investigate the symptoms commonly associated with 14 and 6/sec positive spikes, It should also be noted that these symptoms were compared individually and that no attempt was made to compare symptom complexes.

At the present time, further clinical investigations (preferably prospective) are still necessary to support or reject the hypothesis that even a casual relationship exists between the presence of 14 and 6/sec positive spikes on an EEG and certain symptoms or symptom complexes. In addition, further neurophysiological and neuroanatomical investigations will be necessary to support or reject the hypothesis that a causal relationship is present.

#### SUMMARY and CONCLUSION

A review of the literature dealing with 14 and 6/sec positive spikes and a controlled study of the clinical correlates of 104 patients from the NPI EEG Laboratory who had had EEGs with 14 and 6/sec positive spikes were presented.

The review of the literature included: (a) presentation of the technical aspects of recording 14 and 6/sec positive spikes and a



description of their electroencephalographic appearance, (b) detailed description of the clinical features commonly associated with patients exhibiting 14 and 6/sec positive spikes as derived from a large number of retrospective clinical studies, (c) presentation of several conflicting theoretical discussions and experimental investigations of the neuroanatomical and neurophysiological aspects of 14 and 6/sec positive spikes, and (d) a review of the prospective clinical investigation of Walters et al. who found no significant difference between 4 groups of patients (grouped according to an EEG classification of normal, abnormal, mixed abnormal and 14 and 6/sec positive spikes, and pure 14 and 6/sec positive spikes) in relation to autonomic phenomena, emotional make-up, and behavioral patterns.

The controlled investigation of the clinical correlates of 104 patients referred to the NPI EEG Laboratory who had had EEGs with 14 and 6/sec positive spikes included: (a) description of the electroencephalographic characteristics such as topographical location and frequencies of the positive spikes, other associated EEG abnormalities, and the presence of positive spikes on repeat EEGs, (b) description of the age and sex distribution of the Experimental Group which revealed that 87% of the patients were from 5-20 years of age and that the modal age interval for males

was 10-14 years as compared to a female modal age interval of 15-19 years, and (c) a comparison between the Experimental and the Matched Control Group (composed of 104 patients from the same referral source, who were matched for age and sex with the Experimental Group, but who had had a normal EEG) by means of a "blind" review of the clinical records of both groups and a forced choice check list of symptoms commonly associated with 14 and 6/sec positive spikes.

The data of this experiment did not support the hypothesis that a relationship exists between the presence of 14 and 6/sec positive spikes on an EEG and the presence of symptoms (commonly associated with positive spikes) in the clinical records of patients referred to the NPI EEG Laboratory. The necessity for further clinical (preferably prospective), neurophysiological, and neuro-anatomical investigations was emphasized.

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