

Quantitative Studies of Slow Wave ActivityFollowing Electroshock

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Despite repeated attempts, correlations between slow wave activity induced by electroshock and subsequent therapeutic outcome have been unsuccessful. However, certain conclusions are warranted from previous studies (1). Electroshock therapy induces alterations in the electroencephalogram in all subjects. Three patterns are generally described: 1) slowing of the alpha frequencies; 2) the appearance of random, symmetric slow wave activity, generally of high voltage which may appear as burst activity; and 3) diminution of beta frequencies in rate and amplitude. There is a direct relation between the degree of these changes, and the number and frequency of treatments. In many subjects a saturation point of change is described, which can be maintained by further treatment, but which is apparently not increased. Such induced electroencephalographic changes are reversible. The rate of return of the cerebral patterns to the pretreatment levels is generally 1 to 4 weeks, depending directly on the number, frequency and the type of treatment.

Another area of agreement among the cited authors is the lack of direct relationship between degree of manifest memory loss and confusion and the degree of electroencephalographic abnormality. Cases are described of severe memory changes with few treatments and without significant electroencephalographic change; and also of severe changes in cerebral rhythms without manifest clinical confusion or memory impairment. In these reports, it is stated that such organic confusion also correlates poorly with clinical results.

Two studies, however, may be cited as noting a correlation between electroencephalographic changes and clinical improvement. Hoagland, Malamud, Kaufman and Pincus in their 1946 study of involuntional women (2) reported a relation between changes in their clinical rating scale and the per-cent time more than 13 cycles per second activity. As the disturbed behavior became more manifest, the fast activity increased. As treatment induced behavioral improvement, such fast activity diminished. With recurrence of symptoms, there was an increase in the % time 13 cycles per second activity.

More recently, Roth (3) described a relationship between thiopentone induced EEG changes and the recovery process. Roth noted that slow wave activity as seen in a routine post-shock record was irregular in appearance, and he confirmed the reports that it could not be satisfactorily related to improvement. However, by administering an intravenous solution of the thiopentone, he elicited characteristic changes in the EEG after electroshock in every subject. Early, there was random irregular slow wave activity, which increased with more treatment to a highly rhythmic, bilaterally synchronous, high amplitude delta runs and bursts. These were chiefly 2-3 cycles per second, with voltages of 200-350 microvolts and continuous durations of 30-80 seconds. When the resting record evinced rhythmic delta activity, thiopentone increased its voltage and duration, spread its area, and decreased its basic frequency. Roth believed that these changes were related to the process of recovery, and he concluded: "The development of a typical EEG change does not ensure recovery and 10 of the 36 patients who attained such a change failed to remit for longer than two weeks. But transient improvement in clinical condition seemed to be related to the EEG change even in these patients. If we are correct in connecting the EEG changes with the therapeutic effect it would seem, since most of the patients develop typical changes, that the physiological basis for improvement is acquired by the majority of cases; it may or may not prove effective in promoting recovery."

While these two studies demonstrate a relationship between clinical result and EEG abnormality, the majority of reports fail to do so. It is not likely that this discrepancy is the result of different populations, but rather, the differences in methods of evaluating improvement, the time of evaluation, and differences in estimating changes in cerebral function.

In the course of studies of altered brain function induced by electroshock at the Hillside Hospital in New York, further data on the relationship between EEG changes and clinical effects of electroshock were collected. The general results of previous investigations on the alterations in the EEG with electroshock were confirmed, but also, a definite relationship between EEG effects and the clinical result was demonstrated. Three foci are presented today:

- (1) The EEG patterns following electroshock and their relation to improvement.
- (2) The intercorrelations of different quantifications of delta activity.
- (3) The relation of these observations to a theory of electroshock action.

SUBJECTS AND METHOD: Twenty-four consecutive patients referred for electroshock were studied. Electroencephalograms were done prior to treatment, at weekly intervals during treatment and after treatment. An 8 channel Medcraft instrument, needle electrodes, and bipolar recording was used. Hyperventilation was the only activation technic utilized. During treatment, records were taken the day after, generally 25 to 31 hours after treatment.

The treatments were administered by the staff psychiatrists, using a Reiter C 47 electrostimulator. Treatment schedules were three times a week; and the number of treatments varied from 9 to 33. As patients showed clinical improvement, the psychiatrist tended to give fewer treatments, and more widely

spaced. There were 15 women and 9 men in the series, and ages ranged from 24 to 68 with a median of 47.

EVALUATION OF CLINICAL RESPONSE: All the patients were observed for at least eight weeks after termination of therapy.

The patient's response to electroshock was determined on the basis of the resident psychiatrist's impression, staff opinion, the nurse's notes and the clinical evaluation of the supervisor in charge of electroshock. The patients were divided into three groups - markedly improved, moderately improved and unimproved.

A. Markedly Improved: The 11 cases in this group were regarded as showing recovery or marked improvement. These patients no longer showed the symptoms which brought them into the hospital; their doctor felt they were better; and the nurses' notes confirmed such aspects as being able to sleep without medication, better appetite, and improved capacity to get along with the other patients and participate in hospital activities.

B. Moderately Improved: The six patients in this group showed some improvement but continued to manifest indications of mental illness. These patients typically showed symptomatic relief, i.e., acute depressive features might be gone, but the dramatic change so evident in the first group was not apparent. Each patient continued to show some noticeable disturbance such as obsessional thinking, paranoid ideas, or somatic preoccupation.

C. Minimally or unimproved: In this group were placed seven patients in whom change was not clearly noticeable or who showed only equivocal or transient improvement. Some showed fluctuations in behavior, at times appearing somewhat improved. But the changes were not sustained, so that by the end of treatment, they appeared much as they did before.

We are aware of the difficulties in evaluating improvement. Others might have differed in the estimates of change in these patients. In any case, by using this threefold classification, the differences between the first and third groups will be distinct.

EVALUATION OF EEG RECORDS: A total of 160 records were obtained in these subjects. Following the suggestion of Strauss (4), the delta index was determined for three lead combinations (frontal-parietal, anterior temporal - vertex, and parietal-ear lobe) for 180 seconds of recording for each lead. The delta index is defined as the per-cent time occupied by waves of 7 cps or slower. The average delta-index for the three leads, and the highest delta index in any lead were the indices used in the final tabulation.

Simultaneously, the record was scanned for the slowest frequency identified at least twice in any lead; the highest voltage of any delta wave; and the duration of the longest burst.

On the basis of these five indices of slow wave activity the records were placed in a rank order from the greatest abnormality to the lowest. The 160 records were then divided into 3 groups - i.e. upper third = high degree EEG abnormality, and lowest third = low degree abnormality.

RESULTS: 1. Our results show a positive correlation between early high degree EEG abnormality and improvement. These relationships are demonstrated in Slide I.

By utilizing these quantifications of slow wave abnormality induced by electroshock, we conclude that such EEG abnormality induced in the first 3 weeks of treatment is an essential pre-requisite for the short term favorable clinical response.

2. What relationships exist between each of the indices, first with the clinical response, and then amongst each other?

Similar analyses of the relation of each of the indices and clinical result showed identical curves to the group curve shown before. Slide 2 shows the relation of the delta index to improvement. The mean index in the much improved group jumps to 52% by the 7-9 treatment; while the moderately improved and unimproved groups show a gradual, slow increase to 10-20% by the 10-12 treatment.

A similar set of curves is demonstrated in slide 3 for the mean highest percent time delta in one lead.

In the next slide the mean slowest frequency is recorded, and this, too, shows the same significant relationships. While the much improved patients show delta waves down to 3 cps or less by the second week of treatment, the other two groups rarely reach 4 cps by the fourth week of treatment.

Slide 5 shows the same correlations for the mean highest amplitude, the much improved group show higher voltages by the second week and by the fourth week the differences are persistent for all three groups.

Finally, slide 6 shows the mean duration of bursts. The records of the much improved patients show longer bursts, averaging more than 7 seconds by the third week of treatment. Bursts are less frequent in the unimproved and moderately improved groups and are significantly shorter in duration. Not noted here, however, is the factor of regularity of bursts. In the longer bursts, wave forms frequently were more regular in frequency and amplitude, than in the other two groups.

These studies may be interpreted as demonstrating that each of these measures of slow wave activity arise from the same physiological process, and assume the same significance in relation to the disturbances in cerebral function induced by electroshock.

3. Finally, can these alterations in the EEG be correlated with other aspects of cerebral function which may have been altered by electroshock? In these studies, three other indices of cerebral function were assayed - the amygdala

improvement following electroshock is the result of the creation in the patient of a milieu of altered brain function in which new patterns of adaptation, particularly those of denial, may be maintained. These EEG studies demonstrate that an altered milieu of cerebral function as measured by delta abnormality is a pre-requisite for improvement. To this extent the first part of the Weinstein-Kahn hypothesis is supported.

Secondly, these studies point to the validity of quantitative EEG studies for the elucidation of mechanisms of behavior.

REFERENCES

1. Chusid, Joseph G. and Pacella, Bernard L.: The Electroencephalogram in the Electric Shock Therapies, *J. Nerv. & Ment. Dis.*, 116: 95-107, 1952.
2. Hoagland, H., Malamud, W., Kaufman, and Pincus, G.: Changes in the Electroencephalogram and in the Excretion of 17 Ketosteroids Accompanying Electroshock Therapy of Agitated Depression, *Psychosom. Med.*, 8: 246-251, 1946.
3. Roth, Martin: Changes in the EEG Under Barbiturate Anesthesia Produced by Electroconvulsive Treatment and Their Significance for the Theory of ECT Action, *EEG and Clin. Neurophys.*, 3: 261-280, 1951.
4. Strauss, Hans: Clinical and Electroencephalographic Studies - Correlations of Mental, Electroencephalographic and Anatomic Changes in Cases with Organic Brain Disease, *Am. J. Psychiat.*, 101: 42-50, 1944.
5. Weinstein, E.A., and Kahn, R.L.: Diagnostic Use of Amobarbital Sodium ("Amytal Sodium") in Organic Brain Disease, *Am. J. Psychiat.*, 109: 12, 889-894, 1953.
6. Fink, M., Green, M. and Bender, M.: The Face-Hand Test as a Diagnostic Sign of Organic Mental Syndrome, *Neurology*, 2: 46-58, 1952.
7. Korin, H., Fink, M. and Kwalwasser, S.: Relation of Changes in Memory and Learning to Improvement in Electroshock, *Conf. Neurologica*, 16: 88-96, 1956.
8. Weinstein, E.A., Kahn, R.L. and Linn, L.: Psychosis During Electroshock Therapy: Its Relation to the Theory of Shock Therapy, *Am. J. Psychiat.*, 109: 22-26, 1952.

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Quantitative Studies of Slow Wave Activity Following Electroshock

Despite repeated attempts, correlations between slow wave activity induced by electroshock and subsequent therapeutic outcome have been unsuccessful. Certain conclusions from previous studies are warranted, however. ~~That~~ All patients subjected to electroshock therapy suffer alterations in the electroencephalogram's patterns. ^{These patterns are} Generally described ^{as} ~~the~~ ^{the} 1) The ~~slow~~ slowing of alpha frequencies; 2) The appearance of random, symmetric slow wave activity, generally of high voltage which progresses to burst activity; and 3) diminution of beta frequencies in rate and amplitude. There is a direct relation between the ~~severity of~~ degree of these changes, and the number and frequency of treatment. In many subjects a saturation point of change

(2)

is described, which can be maintained by further treatment, but which, seemingly, is not increased. Also, such electroencephalographic changes are reversible. The rate of return of the cerebral patterns to the pre-treatment levels is generally 1 to 4 weeks, depending directly ^{after} on the number ~~and~~ frequency and the type of treatment.

Another area of agreement amongst the cited authors is the ~~independence~~ lack of direct relationship between degree of manifest memory loss and confusion and the ~~the~~ degree of electroencephalographic abnormality. Cases are cited of severe memory changes with few treatments and without significant electroencephalographic change; and also of severe changes in cerebral rhythms without manifest clinical confusion ^{or} memory impairment. ~~and~~ In these reports, emphasis is frequently ~~made that~~ ^{laid} on such organic confusion also correlating poorly with clinical results.

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~~study~~ study of involuntarily women - (Changes in the Electroencephalogram and in the Excretion of 17 Ketosteroids accompanying Electroshock Therapy of Agitated Depression, Psychom. Med 8: 246-251, (1946)) reported a relation between ~~the~~ their ~~rating~~ clinical rating scale and the percent time 13 cps activity.

As the disturbed behaviour became more manifest, the 13 cps activity increased. As treatment induced behavioural improvement, 13 cps activity diminished. With recurrence of symptoms, there was an increase in the % time 13 cps activity.

More recently, Roth (Changes in the EEG under Barbiturate Anesthesia Produced By Electroconvulsive Treatment and Their Significance for the Theory of ECT Action, EEG and Clin Neurophys 3: 261-280, 1951) described a series of studies in which a relationship between the pentone induced EEG changes and the recovery process ~~were~~ was elicited. ~~When~~ Roth noted that slow wave activity as seen in a routine record was irregular in ~~was reduced~~

(4)

Confirmed the reports that appearance, and he felt it could not be satisfactorily related to improvement. By administering an intravenous solution of a barbiturate, thiopentone, Roth elicited characteristic changes in the EEG after electroshock in every subject. Early there was random, ^{irregular} slow wave activity, which, with more treatment, increased to a highly rhythmic, bilaterally ~~cross~~ synchronous, high amplitude delta runs and bursts. These were chiefly 2-3 cps, with voltages of 200-350 μ v and ^{continuous} durations of ~~170-200~~ ³⁰⁻⁸⁰ seconds. When the resting record showed rhythmic delta activity, thiopentone increased its ^{voltage and} duration, spread its area, and decreased its ^{base} frequency. Roth ^{believed} ~~concluded~~ that these changes were related to the process of recovery, although, he ^{concluded} notes: "copy # pg 275"

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In the course of studies of altered brain function induced by electroshock at the Bellside Hospital in New York, further data ~~on the~~ on the relationships between EEG changes and clinical effects of electroshock were collected. The general results of previous investigators were confirmed, but, on the alterations in the EEG with electroshock were confirmed, but also, a definite relationship between EEG effects and the clinical result was demonstrated. ~~These~~ ~~findings~~ findings are presented today:

- (1) The EEG patterns ~~and~~ following electroshock and their relation to improvement.
- (2) The ~~to~~ intercorrelations of different quantifications of delta activity.
- (3) The relation of these observations to a theory of electroshock therapy action.

(6)

Subjects and Method: Twenty-four consecutive patients referred for electroshock were studied. Electroencephalograms were done prior to treatment and at weekly intervals ~~throughout~~ during and following the course of treatment. An 8-channel Medcraft instrument ~~was used,~~ needle electrodes and bipolar recording was used. Hyperventilation was the only additional technique used. During treatment records were taken on the off day after a treatment, generally 25 to 31 hours after treatment. All treatments were administered by the staff psychiatrist, using a Rectic C47 electrostimulator. Treatment schedules were three times a week; and the number of treatments varied from 9 to 33. As patients showed clinical improvement, the psychiatrist tended to give fewer treatments, and were widely spaced. There were 15 women and 9 men in the series, and the ages ranged from 24 to 68 with a median of 47.

Clinical Evaluation of Response: All the patients were observed for at least eight weeks after termination of therapy. The patient's response to electroshock was made on the basis of

(2)

the resident psychiatrist's impression, staff opinion, the nurse's notes and the clinical evaluation of the supervisor in charge of electroshock. The patients were divided into three groups — markedly improved, moderately improved and unimproved, as to their short term (1-2 months) response to electroshock.

a) Markedly Improved:

b) Moderately Improved

c) Unimproved

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Evaluation of EEG Records: A total of 160 records were ~~collected~~ obtained on these subjects.

~~The records were analyzed~~ classified

Following the suggestion of Dr. Sam Strauss (Clinical and Electroencephalographic Studies - Correlations of Mental, Electroencephalographic and Anatomical Changes in Cases with Organic Brain Disease, Am. J. Psychiat 101: 42-50, 1944), the delta index was determined for three leads (frontal-parietal, anterior temporal-vertex, and parietal-ear lobe) for 180 seconds of recording for each lead. The delta index ~~was the~~

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~~scanned~~ for the slowest frequency identified at least twice in any lead; the highest voltage of any delta wave; and the duration of the longest bursts. Other aspects recorded, but

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not used in the final evaluation, were the regularity of burst activity, slowing of alpha activity, and the degree, ^{frequency} and amplitude of fast activities. These ~~were~~ indices did not lend themselves to statistical study, and were not ~~uniform~~ ~~in all the records~~ identifiable in all the records. Fast activities were readily altered by the ^{clinical} administration of barbiturates. As this medication could not be controlled our evaluations of fast activity ^{following electroshock} are not satisfactory, and the results of Hoagland et al ~~are not confirmed~~ have not been subjected to study here.

On the basis of the five indices of slow wave activity used, - i.e., the average delta index, the highest delta index, the slowest wave, the highest amplitude and the duration of bursts - the records were placed in a rank order ~~of those with greatest abnormality~~ ~~on the top and those with low~~ from the greatest abnormality to the lowest. The 160 records were then divided into 3 groups - i.e. upper third = high degree EEG abnormality;

and lowest third = Low degree abnormality.

~~to~~

Results:

~~1. The first case~~

1. What is the correlation between high degree ^{EEG} abnormality and clinical evaluation of short term (1-2 month) response to electroshock? There was a positive correlation between early ~~high~~ high degree abnormality and improvement. Of the much improved patients, 25% showed a high degree abnormality after one week of treatment; 80% after two weeks and over 90% after 3 weeks. In the unimproved patients, however, none had a ~~to~~ high degree abnormality record during the first 3 weeks and only one had such a record by the fourth week of treatment. The ^{records of the} moderately improved patients fall in between these two groups. These relationships are demonstrated in Slide I.

By utilizing these quantifications of slow wave abnormality induced by electroshock, we conclude that such EEG abnormality

(1)

induced in the first 3 weeks of treatment is essential for ^{the} short term clinical response.

2. What correlations exist between each of the indices, ^{first} with the clinical response, and then amongst each other?

Similar analyses of the relation of each of the indices and clinical result showed identical curves to the group curve shown before. Slide 2 shows the relation of the delta index to improvement. The ^{mean} index in the ^{most} improved group jumps to 52% by the 7-9 treatment; while the moderately improved and unimproved groups show a gradual, slow increase to 10-20% by the 10-12 treatment.

A similar set of curves is demonstrated in slide 3 for the mean highest percent sine delta in one lead.

In the next slide the mean slowest frequency is recorded, and this too shows the same significant relationships. While the most improved parents show delta waves down to

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3 cps or less by the second week of treatment, the other two groups barely reach 4 cps by the fourth week of treatment.

Slide 5 shows the same correlations for the mean highest amplitude. The most improved group show higher voltages by the second week and by the fourth week the differences are persistent for all three groups.

Finally, slide 6 shows the mean duration of burst. The records of the most improved patients show longer bursts, averaging more than 7 seconds by the third week of treatment. Bursts are less frequent in the unimproved and moderately improved groups and are significantly shorter in duration. Not noted here, also, is the factor of regularity of burst. In the long bursts, more frequent, were ^{how} regular in frequency and amplitude, than in the other two groups.

These studies may be interpreted as demonstrating ~~a~~ that each of these measures of slow wave activity arise from the same physiological process, and assume the same significance in relation to the disturbances in cerebral function produced by electroshock.

3. Finally, can these alterations in

the EEG be correlated by with other aspects of cerebral function which may have been altered by electroshock? In these studies, three other indices of ~~altered~~ cerebral function were assayed - the amygdal test of Weinstein and Kalin ~~for~~ the tests of double simultaneous tactile stimulation and ~~memory and~~ test of memory and recall. Of these three indices, only the amygdal test showed a positive correlation with improvement and with the EEG. In this test, the subject is 'reprimed' and questions of orientation, ^{and} insight into illness ~~are~~ are asked. After the administration of subconvulsive sodium amygdal, the questions are repeated. Errors in presentation, confabulation, denial of illness and reduplication are scored as

"Positive" amygdal test and are indicative of cerebral dysfunction. ~~The absence of these tests~~

Correct responses to these questions after amygdal are a 'negative' amygdal test.

In the next slide, #7, the percentage positive amygdal tests are compared for each of the three groups with the number of weeks of treatment. The differences between the much improved and the other two groups is striking. While every patient in the much improved group had a positive amygdal by the end week of treatment and the abnormality persisted; in the unimproved group only one patient had a positive amygdal and this was transient despite continued treatment.

In slide #8 the correlation between the amygdal testing and the EEG high degree ~~an~~ EEG abnormality shows a distinct causal which is statistically significant.

What of the simultaneous tactile tests and the tests of memory and recall? These indices showed no correlation with improvement. In this

respect, it can be concluded that there are various types of cerebral dysfunction and that one cannot speak in gross terms of a lack of correlation between the EEG and cerebral dysfunction or Organic psychosis.

At this point I should like to summarize our findings and express some thoughts as to their significance for cerebral physiology and a theory of electroshock action. There is little doubt that electroshock induces delta abnormality in the EEG. It is symmetric, chiefly frontal, but with increasing treatment, spreads to all leads. With increasing treatment the frequencies become slower, the amplitude higher, the burst activity longer and more regular. While delta abnormality is present in every record after electroshock, its degree and duration is variable. ~~the~~ Roth's experiments inducing increasing delta abnormality with barbiturate are significant ~~in that it points up the fact that abnormality~~ in ~~producing~~ ~~the~~ ~~late~~ ~~stage~~ ^{changes}

reduced by further electroshock. In some subjects, however, a high degree delta abnormality is not induced despite extensive treatment.

Our correlations of degree of delta abnormality with improvement are significant for ^{the mechanism of} electroshock therapy. As early, ^{suggested} alterations in cerebral function as measured by the EEG, and also by the amygdal test, are a necessary pre-requisite for improvement. Where such changes fail to occur in the EEG (and in the amygdal test), then ~~improvement~~ ^{significant} ~~clinical~~ improvement will fail to occur in the patient's behaviour. ~~The converse, however, is not necessary~~

The fact that the correlations were not ~~correlated~~ ~~not~~ memory loss, points to the possibility that this is not a significant factor in improvement.

In conclusion,

These studies lend support to a theory of EST action recently formulated by Moustafa and one of us (Kahn). These authors postulate that improvement following electroshock is the result

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of the creation of in the patient of a milieu of altered brain function in which new patterns of adaptation, particularly those of denial, may be maintained. These EKG studies demonstrate that an altered milieu of cerebral function as measured by delta abnormality is a pre-requisite for improvement. To this extent the first part of the Wernick-Koh hypothesis is supported.

Secondly, these studies point to the significance of quantitative EKG studies for the elucidation of mechanism of behaviour.

Quantitative Studies of Slow Wave Activity

Following Electroshock

Despite repeated attempts, correlations between slow wave activity induced by electroshock and subsequent therapeutic outcome have been unsuccessful. Certain conclusions from previous studies are warranted, however. All patients subjected to electroshock therapy suffer alterations in the electroencephalographic patterns. Three patterns are generally described as 1) the slowing of the alpha frequencies; 2) the appearance of random, symmetric slow wave activity, generally of high voltage which progresses to burst activity; the 3) deminution of beta frequencies in rate and amplitude. There is a direct relation between the degree of these changes, and the number and frequency of treatments. In many subjects a saturation point of change is described, which can be maintained by further treatment, but which, seemingly, is not increased. Also, such electroencephalographic changes are reversible. The rate of return of the cerebral patterns to the pre-treatment levels is generally 1 to 4 weeks, depending directly again on the number, frequency and the type of treatment.

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Presented at the Joint Eastern EEG and Southern EEG
Meeting, Sep 30, 1955 at Bethesda - National Institute of
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medication could not be controlled our evaluations of fast activity following electroshock are not satisfactory, and the results of Hoagland et al, have not been subjected to study here.

On the basis of the few indices of slow wave activity used, - i.e., the average delta index, the highest delta index, the slowest bursts - the records were placed in a rank order from the greatest abnormality to the lowest. The 160 records were then divided into 3 groups - i.e. upper third = high degree EEG abnormality and lowest third = Low degree abnormality.

RESULTS:

1. What is the correlation between high degree EEG abnormality and clinical evaluation of short term (1-2 month) response to electroshock? There was a positive correlation between early high degree abnormality ~~after~~ and improvement. Of the much improved patients, 25% showed a high degree abnormality after one week of treatment; 80% after two weeks and over 90% after 3 weeks. In the unimproved patients, however, none had a high degree abnormality record during the first 3 weeks and only one had such a record by the fourth week of treatment. The records of the moderately improved patients fall in between these two groups. These relationships are demonstrated in Slide I.

By utilizing these quantifications of slow wave abnormality induced by electroshock, we conclude that such EEG abnormality induced in the first 3 weeks of treatment is essential for the short term clinical response.

2. What correlations exist between each of the indices, first with the clinical response, and then among each other?

Similar analyses of the relation of each of the indices and clinical result showed identical curves to the group curve shown before. Slide 2 shows the relation of the delta index to improvement. The mean index in the much improved group jumps to 52% by the 7-9 treatment; while the moderately improved and unimproved groups show a gradual, slow increase to 10-20% by the 10-12 treatment.

A similar set of curves is demonstrated in slide 3 for the mean highest percent time delta in one lead.

In the next slide the mean slowest frequency is recorded, and this too shows the same significant relationships. While the much improved patients show delta waves down to 3 cps or less by the second week of treatment, the other two groups barely reach 4 cps by the fourth week of treatment.

Slide 5 shows the same correlations for the mean highest amplitude. The much improved group show higher voltages by the second week and by the fourth week the differences are persistent for all three groups.

Finally, slide 6 shows the mean duration of bursts. The records of the much improved patients show longer bursts, averaging more than 7 seconds by the third week of treatment. Bursts are less frequent in the unimproved and moderately improved groups and are significantly shorter in duration. Not noted here, also is the factor or regularity of bursts. In the long bursts, wave forms frequently were more regular in frequency and amplitude, than in the other two groups.

These studies may be interpreted as demonstrating that each of these measures of slow wave activity arise from the same physiological process, and assume the same significance in relation to the disturbances in cerebral function induced by electroshock.

3. Finally, can these alterations in the EEG be correlated with other aspects of cerebral function which may have been altered by electroshock? In these studies, three other indices of cerebral function were assayed—the amytal test of Weinstein and Kahn tests of double simultaneous tactile stimulation and tests of memory and recall. Of these three indices, only the amytal test showed a positive correlation with improvement and with the EEG. In this test, the subject is interviewed and questions of orientation of intravenous sodium amytal, the questions are repeated errors in orientation, confabulation, denial of illness and reduplication are scored as "positive" amytal test, and are indicative of cerebral dysfunction. Correct responses to these questions after amytal are a "negative" amytal test.

In the next slide, #7, the percentage positive amytal tests are compared for each of the three groups, with the number of weeks of treatment. The difference between the much improved and the other two groups is striking. While every patient in the much improved group had a positive amytal by the third week of treatment, once the abnormality persisted; in the unimproved groups only one patient had a positive amytal and this was transient despite continued treatment.

In slide # 8, the correlation between the amytal testing and the high degree EEG abnormality shows a distinct correlation which is statistically significant.

What of the simultaneous tactile tests and the tests of memory and recall? These indices showed no correlation with improvement. In this respect, it can be concluded that there are various types of cerebral dysfunction and that one cannot speak in gross terms of a lack of correlation between the EEG and cerebral dysfunction or organic psychoses.

At this point I should like to summarize our findings and express some thoughts as to their significance for a theory of electroshock action. There is little doubt that electroshock induces delta abnormality in the EEG. It is symmetric, chiefly frontal, but with increasing treatment, spreads to all leads. With increasing treatment the frequencies became slower, the amplitudes higher, the burst activity longer and more regular. While delta abnormality is present in every record after electroshock, its degree is variable. Roth's experiment's inducing increasing delta abnormality with barbiturate are significant in predicting the later changes induced by further electroshock. In some subjects however, a high degree delta abnormality is not induced despite extensive treatment.

Our correlations of degree of delta abnormality with improvement are significant for the mechanism of electroshock therapy. An early, sustained alteration in cerebral function as measured by the EEG, and also by the amytal test, are a necessary pre-requisite for improvement. Where such changes fail to occur in the EEG (and in the amytal test), ~~there is~~ a significant clinical improvement will fail to occur in the patient's behavior. The fact that the correlations were not ^{evi}dent with memory loss, points to the possibility that this is not a significant factor in improvement.

In conclusion, these studies lend ~~support to~~ support to a theory of EST action recently enumerated by Weinstein and one of us (Kahn). These authors postulated that improvement following electroshock is the result of the creation in the patient of a milieu of altered brain function in which new patterns of adaptation, particularly those of denial, may be maintained. These EEG studies demonstrate that an altered milieu of cerebral function as measured by delta abnormality is a pre-requisite for improvement. To this extent the first part of the Weinstein-Kahn hypothesis is supported.

Secondly, these studies point to the significance of quantitative EEG studies for the elucidation of mechanisms of behavior.

To: Dr. Joseph S. A. Miller.

From: Dr. Max Fink

May I have your approval to submit
this technical paper to the Eastern
EEG Society for its October meeting in
Bethesda ?

Max Fink
2/25/55

July 25, 1955

Quantitative Studies of Slow Wave Activity Following Electroshock *

Max Pink, M.D.

Robert L. Kahn, Ph. D.

In the course of an investigation of altered brain function following electroshock, various measures of slow wave activity were correlated with alteration in behaviour. Electroencephalograms were done on 24 consecutive patients referred for electroshock therapy. Records were taken prior to and at weekly intervals during and following the course of treatment. The total of 160 records so obtained were classified according to five criteria: the average per-cent time slow waves (7 cps or less) for three given lead combinations (frontal-parietal, anterior temporal-vertex, and parietal-ear lobe), the highest per-cent time slow wave in any one lead combination, the lowest slow wave frequency, the duration of the longest bursts and the highest slow wave amplitude. On the basis of percentile scores obtained for each factor, the relative position of each record was determined. Those in the upper third of the distribution were considered to have high degree abnormality, while those in the lower third were low degree abnormality. Ratings of degree of alteration in behaviour were made by the supervising psychiatrist and the patients were characterized as "much improved," "improved," and "unimproved."

The following correlations were significant:

(1) A positive correlation between degree of alteration in behaviour and degree of EEG abnormality was demonstrated. Of the much improved patients, 25% showed high degree EEG abnormality after one week of treatment, 80% after two weeks and over 90% after three weeks. In the unimproved patients, however, none had a high degree abnormality record during the first three weeks and

only one had such a record by the fourth week of treatment.

(2) Analyzing the relation of altered behaviour to each of the measures of slow wave activity, demonstrates a positive correlation for each index.

(3) Each of the indices of slow wave activity were significantly correlated with each other.

The significance of these observations for electroshock therapy, and the validity of these indices in electroshock studies will be discussed.

orig¹ d.s.

Quantitative Studies of Slow Wave Activity
Following Electroshock

Max Fink, M.D.

Robert L. Kahn, Ph.D.

Hillside Hospital, Glen Oaks, New York

subjects.

Despite repeated attempts, correlations between slow wave activity induced by electroshock and subsequent therapeutic outcome have been unsuccessful. However, certain conclusions ⁽¹⁾ from previous studies ⁽²⁾ are warranted. All patients ~~sub-~~ ^{induces} jected to Electroshock therapy suffer alterations in the electroencephalogram, *in all* subjects. Three patterns are generally described: as 1) ~~the~~ slowing of the alpha frequencies; 2) the appearance of random, symmetric slow wave activity, generally of high voltage which ^{may appear as} progresses to burst activity; and 3) diminution of beta frequencies in rate and amplitude. There is a direct relation between the degree of these changes, and the number and frequency of treatments. In many subjects a saturation point of change is described, which can be maintained by further treatment, but which ~~seemingly~~ ^{apparently} is not increased. ~~Also,~~ ^{reduced} such electroencephalographic changes are reversible. The rate of return of the cerebral patterns to the pretreatment levels is generally 1 to 4 weeks, ^{de} pending directly ~~again~~ on the number, frequency and the type of treatment.

Another area of agreement among the cited authors is the lack of direct relationship between degree of manifest memory loss and confusion and the degree of electroencephalographic abnormality. Cases are described ^{of} severe memory changes with few treatments and without significant electroencephalographic change; and also of severe changes in cerebral rhythms without manifest clinical confusion or memory impairment. In these reports, ^{it} emphasis is ^{stated that} frequently laid on such organic confusion also correlat^{es} poorly with clinical results.

Two studies, however, may be cited as noting a correlation between ^gElectroencephalographic changes and clinical improvement. Hoagland, ^HMalamud, ^{W.}Kaufman and Pincus in their 1946 study of involuntional women ⁽²⁾ - (~~changes in the electroencephalogram and in the excretion of 17 ketosteroids accompanying electroshock therapy of agitated depression, Psychosom. Med. 8: 246-251, 1946~~) reported a relation between changes in their clinical rating scale and the per-cent time more than 13 ^{cycles per second} activity. As the disturbed behavior became more manifest, the ~~13 cps~~ ^{fast} activity increased. As treatment induced behavioral improvement, ~~13 cps~~ ^{such} activity diminished. With recurrence of symptoms, there was an increase in the % time 13 ^{cycles per second} activity.

More recently, ^{(3) Martin} Roth (~~Changes in the EEG under Barbiturate Anesthesia Produced by Electroconvulsive Treatment and Their Significance for the Theory of ECT action, EEG and Clin. Neurophys. 3: 261-280, 1951~~) described a relationship between thopentone induced EEG changes and the recovery process. Roth noted that slow wave activity as seen in a routine post-shock record was irregular in appearance, and he confirmed the reports that it could not be satisfactorily related to improvement. However, by administering an intravenous solution of the ~~barbiturate~~ ^Nthiopentone, he elicited characteristic changes in the EEG after electroshock in every subject. Early, there was random irregular slow wave activity, which, with more treatment, increased to a highly rhythmic, bilaterally synchronous, high amplitude delta runs and bursts. These were chiefly 2-3 ^{cycles per second} ~~cps~~, with voltages of 200-350 ^{MICROVOLTS} ~~mv~~ and continuous durations of 30-80 seconds. When the resting record evinced rhythmic delta activity, thiopentone increased its voltage and duration, spread its area, and decreased its basic frequency. Roth believed that these changes were related to the process of recovery, and

he concluded: "The development of a typical EEG change does not ensure recovery and 10 of the 36 patients who attained such a change failed to remit for longer than two weeks. But transient improvement in clinical condition seemed to be related to the EEG change even in these patients. If we are correct in connecting the EEG changes with the therapeutic effect it would seem, since most of the patients develop typical changes, that the physiological basis for improvement is acquired by the majority of cases; it may or may not prove effective in promoting recovery."

~~While these two studies demonstrate~~ a relationship between clinical result and EEG abnormality, the majority of reports fail to do so. It is not likely that this discrepancy is the result of different populations, but rather, the differences in methods of evaluating improvement, the time of evaluation, and differences in estimating changes in cerebral function.

In the course of studies of altered brain function induced by electroshock at the Hillside Hospital in New York, further data on the relationship between EEG changes and clinical effects of electroshock were collected. The general results of previous investigations on the alterations in the EEG with electroshock were confirmed, but also, a definite relationship between EEG effects and the clinical result was demonstrated. Three foci are presented today:

- (1) The EEG patterns following electroshock and their relation to improvement.
- (2) The intercorrelations of different quantifications of delta activity.
- (3) The relation of these observations to a theory of electroshock action.

SUBJECTS AND METHOD: Twenty-four consecutive patients referred for electroshock were studied. Electroencephalograms were done prior to treatment, at weekly intervals during treatment and after treatment. An 8 channel

but the dramatic change so evident in the first group was not apparent. Each patient continued to show some noticeable disturbance such as obsessional thinking, paranoid ideas, or somatic preoccupation.

C. Minimally or Unimproved: In this group were placed seven patients in whom change was not clearly noticeable or who showed only equivocal or transient improvement. Some showed fluctuations in behavior, at times appearing somewhat improved. But the changes were not sustained, so that by the end of treatment, they appeared much as they did before.

We are aware of the difficulties in evaluating improvement. Others might have differed in the estimates of change in these patients. In any case, by using this threefold classification, the differences between the first and third groups will be distinct.

EVALUATION OF EEG RECORDS: A total of 160 records were obtained in these subjects. Following the suggestion of ~~Dr. Hans~~ Strauss (4) (~~Clinical and Electroencephalographic Studies - Correlations of Mental, Electroencephalographic and Anatomic Changes in Cases with Organic Brain Disease, Am. J. Psychiat. 101: 42-50, 1944~~), the delta index was determined for three lead combinations (frontal-parietal, anterior temporal - vertex, and parietal-ear lobe) for 180 seconds of recording for each lead. The delta index is defined as the per-cent time occupied by waves of 7 cps or slower. The average delta-index for the three leads, and the highest delta index in any lead were the indices used in the final tabulation.

Simultaneously, the record was scanned for the slowest frequency identified at least twice in any lead; the highest voltage of any delta wave; and the duration of the longest burst.

Medcraft instrument, needle electrodes, and bipolar recording was used. Hyperventilation was the only activation technic utilized. During treatment, records were taken the day after, generally 25 to 31 hours after treatment.

The treatments were administered by the staff psychiatrists, using a Reiter C 47 electrostimulator. Treatment schedules were three times a week; and the number of treatments varied from 9 to 33. As patients showed clinical improvement, the psychiatrist tended to give fewer treatments, and more widely spaced. There were 15 women and 9 men in the series, and ages ranged from 24 to 68 with a median of 47.

EVALUATION OF CLINICAL RESPONSE: All the patients were observed for at least eight weeks after termination of therapy.

The patient's response to electroshock was determined on the basis of the resident psychiatrist's impression, staff opinion, the nurse's notes and the clinical evaluation of the supervisor in charge of electroshock. The patients were divided into three groups - markedly improved, moderately improved and unimproved.

A. Markedly Improved: The 11 cases in this group were regarded as showing recovery or marked improvement. These patients no longer showed the symptoms which brought them into the hospital; their doctors felt they were better; and the nurses' notes confirmed such aspects as being able to sleep without medication, better appetite, and improved capacity to get along with the other patients and participate in hospital activities.

B. Moderately Improved: The six patients in this group showed some improvement but continued to manifest indications of mental illness. These patients typically showed symptomatic relief, ie., acute depressive features might be gone,

On the basis of these five indices of slow wave activity the records were placed in a rank order from the greatest abnormality to the lowest. The 160 records were then divided into 3 groups - ~~the~~^{the} upper third = high degree EEG abnormality, and lowest third = low degree abnormality.

RESULTS: 1. Our results show a positive correlation between early high degree EEG abnormality and improvement. These relationships are demonstrated in Slide I.

By utilizing these quantifications of slow wave abnormality induced by electroshock, we conclude that such EEG abnormality induced in the first 3 weeks of treatment is an essential pre-requisite for the short term favorable clinical response.

2. What relationships exist between each of the indices, first with the clinical response, and then amongst each other?

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These studies may be interpreted as demonstrating that each of these measures of slow wave activity arise from the same physiological process, and assume the same significance in relation to the disturbances in cerebral function induced by electroshock.

3. Finally, can these alterations in the EEG be correlated with other aspects of cerebral function which may have been altered by electroshock? In these studies, three other indices of cerebral function were assayed - the amytal test of Weinstein and Kahn,⁽⁵⁾ tests of double simultaneous tactile stimulation,⁽⁶⁾ and tests of memory and recall.⁽⁷⁾ Of these three indices, only the amytal test showed a positive correlation with improvement and with the EEG. These results were presented recently at the American Psychiatric Association and we will forgo a discussion at this time. ←

It ^{may} suffice that the next slide, # 7 demonstrates the correlation between the amytal testing and the high degree ^{of} EEG abnormality. ^{Responses on} this ^{Graph} slide shows a distinct relationship between the two factors.

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inducing increasing delta abnormality with barbiturate are significant in predicting the later changes induced by further electroshock. In some subjects however, a high degree delta abnormality is not induced despite extensive treatment.

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EEG in EST

September 21, 1955

MEMORANDUM

TO: Dr. Joseph S. A. Miller

FROM: Dr. Max Fink

(1) Our paper entitled "Quantitative Studies of Slow Wave Activity Following Electroshock" will be presented at the Eastern EEG meeting at Bethesda, Friday September 30th.

(2) May I have permission for Dr. Kahn (the co-author) and myself to attend the sessions of the society?

Gray
P.C. J. Miller
9/21/55
Expenses chargeable
to U.S. P. W.
Funds.
JBF

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Following Electroshock

Max Fink, M.D.

Robert L. Kahn, Ph.D.

Hillside Hospital, Glen Oaks, New York

Despite repeated attempts, correlations between slow wave activity induced by electroshock and subsequent therapeutic outcome have been unsuccessful. However, certain conclusions are warranted from previous studies (1). Electroshock therapy induces alterations in the electroencephalogram in all subjects. Three patterns are generally described: 1) slowing of the alpha frequencies; 2) the appearance of random, symmetric slow wave activity, generally of high voltage which may appear as burst activity; and 3) diminution of beta frequencies in rate and amplitude. There is a direct relation between the degree of these changes, and the number and frequency of treatments. In many subjects a saturation point of change is described, which can be maintained by further treatment, but which is apparently not increased. Such induced electroencephalographic changes are reversible. The rate of return of the cerebral patterns to the pretreatment levels is generally 1 to 4 weeks, depending directly on the number, frequency and the type of treatment.

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These studies may be interpreted as demonstrating that each of these measures of slow wave activity arise from the same physiological process, and assume the same significance in relation to the disturbances in cerebral function induced by electroshock.

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test of Weinstein and Kahn (5), tests of double simultaneous tactile stimulation (6), and tests of memory and recall (7). Of these three indices, only the amy-tal test showed a positive correlation with improvement and with the EEG. These results were presented recently at the American Psychiatric Association and we will forgo a discussion at this time. It may suffice that the next slide, # 7, demonstrates the correlation between the responses on amy-tal tests and the degree of EEG abnormality. This graph shows a distinct relationship between the two factors.

At this point I should like to summarize our findings and express some thoughts as to their significance for a theory of electroshock action. There is little doubt that electroshock induces delta abnormality in the EEG. It is symmetric, chiefly frontal, but with increasing treatment, spreads to all leads. With increasing treatment the frequencies became slower, the amplitudes higher, the burst activity longer and more regular. While delta abnormality is present in every record after electroshock, its degree is variable. Roth's experiment's inducing increasing delta abnormality with barbiturate are significant in predicting the later changes induced by further electroshock. In some subjects however, a high degree delta abnormality is not induced despite extensive treatment.

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In conclusion, these studies lend support to a theory of EST action recently enumerated by Weinstein and one of us (Kahn) (8). These authors postulated that

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REFERENCES

1. Chusid, Joseph G. and Pacella, Bernard L.: The Electroencephalogram in the Electric Shock Therapies, *J. Nerv. & Ment. Dis.*, 116: 95-107, 1952.
2. Hoagland, H., Malamud, W., Kaufman, and Pincus, G.: Changes in the Electroencephalogram and in the Excretion of 17 Ketosteroids Accompanying Electroshock Therapy of Agitated Depression, *Psychosom. Med.*, 8: 246-251, 1946.
3. Roth, Martin: Changes in the EEG Under Barbiturate Anesthesia Produced by Electroconvulsive Treatment and Their Significance for the Theory of ECT Action, *EEG and Clin. Neurophys.*, 3: 261-280, 1951.
4. Strauss, Hans: Clinical and Electroencephalographic Studies - Correlations of Mental, Electroencephalographic and Anatomic Changes in Cases with Organic Brain Disease, *Am. J. Psychiat.*, 101: 42-50, 1944.
5. Weinstein, E.A., and Kahn, R.L.: Diagnostic Use of Amobarbital Sodium ("Amytal Sodium") in Organic Brain Disease, *Am. J. Psychiat.*, 109: 12, 889-894, 1953.
6. Fink, M., Green, M. and Bender, M.: The Face-Hand Test as a Diagnostic Sign of Organic Mental Syndrome, *Neurology*, 2: 46-58, 1952.
7. Korin, H., Fink, M. and Kwalwasser, S.: Relation of Changes in Memory and Learning to Improvement in Electroshock, *Conf. Neurologica*, 16: 88-96, 1956.
8. Weinstein, E.A., Kahn, R.L. and Linn, L.: Psychosis During Electroshock Therapy: Its Relation to the Theory of Shock Therapy, *Am. J. Psychiat.*, 109: 22-26, 1952.

test of Weinstein and Kahn (5), tests of double simultaneous tactile stimulation (6), and tests of memory and recall (7). Of these three indices, only the amy-tal test showed a positive correlation with improvement and with the EEG. These results were presented recently at the American Psychiatric Association and we will forgo a discussion at this time. It may suffice that the next slide, # 7, demonstrates the correlation between the responses on amy-tal tests and the degree of EEG abnormality. This graph shows a distinct relationship between the two factors.

At this point I should like to summarize our findings and express some thoughts as to their significance for a theory of electroshock action. There is little doubt that electroshock induces delta abnormality in the EEG. It is symmetric, chiefly frontal, but with increasing treatment, spreads to all leads. With increasing treatment the frequencies became slower, the amplitudes higher, the burst activity longer and more regular. While delta abnormality is present in every record after electroshock, its degree is variable. Roth's experiment's inducing increasing delta abnormality with barbiturate are significant in pre-dicting the later changes induced by further electroshock. In some subjects however, a high degree delta abnormality is not induced despite extensive treat-ment.

Our correlations of degree of delta abnormality with improvement are also significant for the theory of the mechanism of electroshock. An early, sus-tained alteration in cerebral function as measured by the EEG, and also by the amy-tal test, appears to be a necessary pre-requisite for improvement. Where such changes fail to occur in the EEG (and in the amy-tal test), then significant clinical improvement will fail to occur in the patient's behavior. The fact that the correlations were not ivident with memory loss, points to the possibility that this is not a significant factor in improvement.

In conclusion, these studies lend support to a theory of EST action recently enumerated by Weinstein and one of us (Kahn) (8). These authors postulated that